WEST Search History

DATE: Friday, September 12, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L18	L13 and gmpwlsattvrsvthanalt	1	L18
L17	L13 and msp1	22	L17
L16	L14 and svthanaltvmgkastpgaa	1	L16
L15	L14 and gmpwlsattvrsvthanalt	1	L15
L14	L13 and band 3	25	L14
L13	L12 and (erythroid or erythrocyte)	865	L13
L12	malaria and plasmodium	2674	L12
L11	l8 and band 3	3	L11
L10	l8	43	L10
L9	L8 and malaria	3	L9
L8	l2 or l4 or l5 or l6 or l7	43	L8
L7	li-xuerong.in.	1	L7
L6	goel-vikas.in.	2	L6
L5	oh-s-steven.in.	2	L5
L4	liu-david.in.	42	L4
L3	lui-david.in.	0	L3
L2	chishti-athar-h.in.	3	L2
L1	chishti-athar.in.	0	L1

END OF SEARCH HISTORY

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NEWS 4	Feb 24	TEMA now available on STN
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NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation
NEWS 38	AUG 18	Simultaneous left and right truncation added to ANABSTR

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 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
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=> e chishti athar h/au
E1            1     CHISHTI ASIF S/AU
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E2            2     LIU DAVE Q/AU
E3           87 --> LIU DAVID/AU
E4           17     LIU DAVID C/AU
E5            7     LIU DAVID D/AU
E6            3     LIU DAVID D W/AU
E7            4     LIU DAVID H/AU
E8            6     LIU DAVID H F/AU
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E6          245     OH S W/AU
E7          627     OH S Y/AU
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E12           1     OH SAE HEON/AU

=> s e2-e3
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E3           11 --> GOEL VIKAS/AU
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E7            9     GOEL VINAY/AU
E8            1     GOEL VINEET/AU
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E3           50 --> LI XUERONG/AU
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E6            3     LI XUESHEN/AU
E7            3     LI XUESHENG/AU
E8            1     LI XUESHONG/AU
E9            5     LI XUESHU/AU
E10           1     LI XUESHUN/AU
E11          22     LI XUESONG/AU
E12           1     LI XUESUN/AU

=> s e3
L5           50 "LI XUERONG"/AU

=> s l1-l5
L6          514 (L1 OR L2 OR L3 OR L4 OR L5)

=> s l6 and malaria
L7           57 L6 AND MALARIA

=> s l7 and band 3
L8           20 L7 AND BAND 3

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9            9 DUP REM L8 (11 DUPLICATES REMOVED)

=> d bib ab 1-9

L9   ANSWER 1 OF 9  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
     DUPLICATE 1
AN   2003:298699  BIOSIS
DN   PREV200300298699
TI   Band 3 is a host receptor binding merozoite surface
     protein 1 during the Plasmodium falciparum invasion of erythrocytes.
AU   Goel, Vikas K.; Li, Xuerong; Chen, Huiqing; Liu,
     Shih-Chun; Chishti, Athar H. (1); Oh, Steven S. (1)
CS   (1) Department of Medicine, St. Elizabeth's Medical Center, 736 Cambridge
     Street, Boston, MA, 02135, USA: athar.chishti@tufts.edu,
     steven.oh@tufts.edu USA
SO   Proceedings of the National Academy of Sciences of the United States of
```

America, (April 29 2003) Vol. 100, No. 9, pp. 5164-5169. print.
ISSN: 0027-8424.

DT Article

LA English

AB We report the molecular identification of a sialic acid-independent host-parasite interaction in the Plasmodium falciparum **malaria** parasite invasion of RBCs. Two nonglycosylated exofacial regions of human **band 3** in the RBC membrane were identified as a crucial host receptor binding the C-terminal processing products of merozoite surface protein 1 (MSP1). Peptides derived from the receptor region of **band 3** inhibited the invasion of RBCs by P. falciparum. A major segment of the **band 3** receptor (5ABC) bound to native MSP142 and blocked the interaction of native MSP142 with intact RBCs in vitro. Recombinant MSP119 (the C-terminal domain of MSP142) bound to 5ABC as well as RBCs. The binding of both native MSP142 and recombinant MSP119 was not affected by the neuraminidase treatment of RBCs, but sensitive to chymotrypsin treatment. In addition, recombinant MSP138 showed similar interactions with the **band 3** receptor and RBCs, although the interaction was relatively weak. These findings suggest that the chymotrypsin-sensitive MSP1-**band 3** interaction plays a role in a sialic acid-independent invasion pathway and reveal the function of MSP1 in the Plasmodium invasion of RBCs.

L9 ANSWER 2 OF 9 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 2

AN 2002-759814 [82] WPIDS

DNC C2002-214730

TI New isolated **Band 3** polypeptide which selectively binds to merozite surface protein-1, useful for the prevention and treatment of malarial infection.

DC B04 D16

IN CHISHTI, A H; GOEL, V; LI, X; LIU, D; **OH, S S**

PA (SELI-N) ST ELIZABETH'S MEDICAL CENT INC

CYC 29

PI WO 2002070542 A2 20020912 (200282)* EN 163p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU BR CA CN IN JP KR SG ZA
US 2003059436 A1 20030327 (200325)

ADT WO 2002070542 A2 WO 2002-US6415 20020301; US 2003059436 A1 Provisional US 2001-272930P 20010302, US 2002-87464 20020301

PRAI US 2001-272930P 20010302; US 2002-87464 20020301

AB WO 200270542 A UPAB: 20021220
NOVELTY - An isolated **Band 3** polypeptide (I) comprises any of 4 20 residue amino acid sequences, given in the specification, or their fragments that bind to an MSP-1 polypeptide or a polypeptide with any of 8 291-1331 base pair sequences, given in the specification, and exclude the sequences of **Band 3** Blast Homology, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid molecule that encodes (I);

(2) an expression vector comprising the isolated nucleic acid of (1) operably linked to a promoter;

(3) a host cell transfected or transformed with an expression vector of (2);

(4) an immunogenic composition comprising one or more of (I), and a carrier, where (I) induces an immune system response;

(5) making a medicament comprising placing one or more of (I) in a carrier;

(6) identifying a candidate mimetic of (I);

(7) a protein microarray;

(8) an anti-**Band 3** antibody or fragment that selectively binds to (I), where the antibody inhibits infection of cells by Plasmodium falciparum merozite **malaria** parasite;

(9) an anti-idiotype antibody which selectively binds to the antibody of (8);

(10) making an anti-idiotypic antibody;

(11) treating **malaria** infection comprising administering an anti-**Band 3** antibody of (8) to treat **malaria** infection;

(12) inducing an immune system response to treat a **malaria** infection;

(13) identifying a candidate mimetic of a MSP-1 polypeptide;

(14) an isolated polypeptide comprising a 378, 360, 220, 334, 376 or 114 residue amino acid sequence, given in the specification, or their fragments;

(15) a pharmaceutical composition comprising one or more of the polypeptide of (14) and a carrier, where the polypeptides are present to induce an immune system response;

(16) making a medicament comprising placing one or more of the polypeptide of (14) in a carrier;

(17) preventing or treating **malaria** infection comprising administering a pharmaceutical composition of (15) to prevent or treat the **malaria** infection;

(18) a **malaria** polypeptide binding polypeptide that selectively binds to the isolated **malaria** polypeptide of (14), where the binding polypeptide is an antibody or an antigen-binding fragment of an antibody;

(19) a pharmaceutical composition comprising the **malaria** polypeptide binding polypeptide of (18) in a carrier;

(20) preventing or treating **malaria** infection comprising administering a pharmaceutical composition of (19) to prevent or treat the **malaria** infection;

(21) an isolated nucleic acid comprising a 1137, 1080, 660, 1080, 1131 or 343 base pair sequence, given in the specification, or their fragments;

(22) an isolated **Band 3** polypeptide;

(23) an isolated nucleic acid molecule that encodes the isolated polypeptide of (22);

(24) an expression vector comprising the isolated nucleic acid of (23) operably linked to a promoter;

(25) a host cell transfected or transformed with an expression vector of (24);

(26) an immunogenic composition comprising one or more of the isolated polypeptide of (22), and a carrier, where the polypeptide induces an immune system response;

(27) making a medicament comprising placing one or more of the isolated polypeptide of (22) in a carrier;

(28) identifying a candidate mimetic of an isolated malaria polypeptide;

(29) identifying a candidate mimetic of an isolated Band 3 polypeptide of (22);

(30) an isolated polypeptide molecule comprising any of 7 291-1331 base pair sequences, all given in the specification;

(31) a pharmaceutical composition comprising one or more of the polypeptide of (30), and a carrier, where the polypeptides are present to induce an immune system response;

(32) making a medicament comprising placing one or more isolated polypeptide of (30) in a carrier;

(33) treating or preventing a malaria infection comprising administering a pharmaceutical composition of (31);

(34) a malaria polypeptide binding polypeptide that selectively binds to the isolated malaria polypeptide of (30), where the binding polypeptide is an antibody or an antigen-binding fragment of an antibody;

(35) a pharmaceutical composition comprising the malaria polypeptide binding polypeptide of (34) in a carrier;

(36) preventing or treating malaria infection comprising

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 15:01:16 ON 12 SEP 2003

E CHISHTI ATHAR H/AU
L1 126 S E2-E3
E LIU DAVID/AU
L2 87 S E3
E OH S STEVEN/AU
L3 252 S E2-E3
E GOEL VIKAS/AU
L4 24 S E3-E5
E LI XUERONG/AU
L5 50 S E3
L6 514 S L1-L5
L7 57 S L6 AND MALARIA
L8 20 S L7 AND BAND 3
L9 9 DUP REM L8 (11 DUPLICATES REMOVED)

=> s l7 and msp1
L10 11 L7 AND MSP1

=> s l10 and (band 3 or erythroid or erythrocyte)
L11 9 L10 AND (BAND 3 OR ERYTHROID OR ERYTHROCYTE)

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12 4 DUP REM L11 (5 DUPLICATES REMOVED)

=> d bib ab 1-4

L12 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
AN 2003:298699 BIOSIS
DN PREV200300298699
TI **Band 3** is a host receptor binding merozoite surface protein 1 during the Plasmodium falciparum invasion of erythrocytes.
AU **Goel, Vikas K.**; **Li, Xuerong**; Chen, Huiqing; Liu, Shih-Chun; **Chishti, Athar H. (1)**; Oh, Steven S. (1)
CS (1) Department of Medicine, St. Elizabeth's Medical Center, 736 Cambridge Street, Boston, MA, 02135, USA: athar.chishti@tufts.edu, steven.oh@tufts.edu USA
SO Proceedings of the National Academy of Sciences of the United States of America, (April 29 2003) Vol. 100, No. 9, pp. 5164-5169. print. ISSN: 0027-8424.
DT Article
LA English
AB We report the molecular identification of a sialic acid-independent host-parasite interaction in the Plasmodium falciparum **malaria** parasite invasion of RBCs. Two nonglycosylated exofacial regions of human **band 3** in the RBC membrane were identified as a crucial host receptor binding the C-terminal processing products of merozoite surface protein 1 (**MSP1**). Peptides derived from the receptor region of **band 3** inhibited the invasion of RBCs by P. falciparum. A major segment of the **band 3** receptor (5ABC) bound to native MSP142 and blocked the interaction of native MSP142 with intact RBCs in vitro. Recombinant MSP119 (the C-terminal domain of MSP142) bound to 5ABC as well as RBCs. The binding of both native MSP142 and recombinant MSP119 was not affected by the neuraminidase treatment of RBCs, but sensitive to chymotrypsin treatment. In addition, recombinant MSP138 showed similar interactions with the **band 3** receptor and RBCs, although the interaction was relatively weak. These findings suggest that the chymotrypsin-sensitive **MSP1**-**band 3** interaction plays a role in a sialic acid-independent invasion pathway and reveal the function of **MSP1**

in the Plasmodium invasion of RBCs.

L12 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:696001 CAPLUS
DN 137:231370
TI **Erythroid band 3** antigenic peptides, MSP-1 protein and Plasmodium polypeptides for preventing invasion of **malaria** parasite into erythrocytes
IN **Chishti, Athar H.; Oh, S. Steven; Liu, David ; Goel, Vikas**
PA St. Elizabeth's Medical Center, Inc., USA
SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002070542	A2	20020912	WO 2002-US6415	20020301
	WO 2002070542	A3	20030605		
	W: AU, BR, CA, CN, IN, JP, KR, SG, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	US 2003059436	A1	20030327	US 2002-87464	20020301
PRAI	US 2001-272930P	P	20010302		

AB The invention provides peptides derived from **erythroid Band 3** protein, which selectively bind to merozoite surface protein-1 (MSP-1), and/or one or more of the **malaria** polypeptides: BBP-1, BBP-2, BBP-3, BBP-4, BBP-5, BBP-6, RhopH3, and ABRA and prevent infection by the parasite of a **Band 3** -expressing cell, such as an **erythrocyte**. The invention also provides the isolated polypeptides BBP-1, BBP-2, BBP-3, BBP-4, BBP-5, BBP-6, RhopH3, and/or ABRA as well as peptides derived from MSP-1, which selectively bind to **erythroid Band 3** protein and prevent parasite invasion into a **Band 3**-expressing cell, and prevent Plasmodium infection. Methods of using the **malaria** and **MSP1** polypeptides of the invention for **malaria** prevention and/or treatment (e.g. in vaccines) are also provided. Antibodies that bind to the **Band 3** polypeptides and anti-idiotypic antibodies thereto also are provided. Methods for selecting agents which inhibit **Band 3** -mediated parasite entry into target cells and methods of treatment which involve the polypeptides, antibodies, and anti-idiotypic antibodies also are provided.

L12 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:335437 BIOSIS
DN PREV200300335437
TI **Band 3** Interacts with the **Malaria** Parasite Merozoite Surface Protein-1 by a Sialic Acid-Independent and Chymotrypsin-Sensitive Mechanism.
AU Oh, Steven S. (1); **Li, Xuerong (1)**; **Goel, Vikas K. (1)** ; Chen, Huiqing (1); Liu, David S. -C. (1); **Chishti, Athar H. (1)**
CS (1) Departments of Medicine, Anatomy, and Cellular Biology, St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA, USA USA
SO Blood, (November 16 2002) Vol. 100, No. 11 , pp. Abstract No. 837. print. Meeting Info.: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002 American Society of Hematology . ISSN: 0006-4971.
DT Conference
LA English
AB Development of an effective subunit vaccine against blood-stage

malaria requires a precise description of mechanism by which merozoites invade host red blood cells (RBCs). In Plasmodium falciparum **malaria**, RBC invasion is thought to proceed via two distinct routes: sialic acid-dependent and sialic acid-independent pathways. The former invasion pathway involves the interaction of the parasite ligand, EBA-175, with the sialic acid residues of host glycophorin A (GPA). Cumulative evidence using laboratory strains of P. falciparum indicate that this invasion pathway is dispensable and field isolates of P. falciparum commonly use alternate invasion pathways that do not depend on the sialic acid residues of GPA. The sialic acid-independent pathway is influenced by the trypsin-sensitive and/or chymotrypsin-sensitive RBC receptor(s). However, the molecular identity of these receptors has not been established. Recently, we have shown that the 42 kDa proteolytic fragment of P. falciparum merozoite surface protein-1 (MSP142) and its 19 kDa C-terminal domain (MSP119) bind to two non-glycosylated ectodomains of human RBC **band 3** termed 5ABC and 6A by a sialic acid-independent mechanism. Peptides derived from these ectodomains of **band 3** blocked the P. falciparum invasion of RBCs in vitro. Published evidence indicates that MSP119 plays an essential role in the blood-stage parasite development and is functionally conserved between the human and murine **malaria** parasite species. Here, we show that native P. falciparum MSP142 binds to the recombinant 5ABC peptide of **band 3** as well as to intact human RBCs in suspension. The binding of native MSP142 to RBCs was drastically reduced when 5ABC was added to the binding reaction mixture. Furthermore, native MSP142 bound to trypsin-treated, and neuraminidase-treated RBCs, but not to chymotrypsin-treated RBCs. We also show that recombinant MSP119 derived from the murine **malaria** species, P. yoelii, which shares 37% sequence identity with P. falciparum MSP119, binds to both mouse and human intact RBCs. The chymotrypsin treatment of both RBC types showed a marked reduction in binding to P. yoelii MSP119, while the neuraminidase treatment had no effect on the binding capacity. Moreover, P. yoelii MSP119 bound to 5ABC (human sequence) that shares 98% identity with the mouse **band 3** sequence. Together, our results suggest that **band 3** is a chymotrypsin-sensitive and trypsin-insensitive RBC receptor binding the 42 kDa and 19 kDa processing products of **MSP1** during **malaria** parasite invasion of erythrocytes.

L12 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:209830 BIOSIS
DN PREV200200209830
TI **Band 3** is a host receptor for **malaria** parasite Plasmodium falciparum invasion of red blood cells.
AU **Oh, S. Steven (1)**; **Goel, Vikas K. (1)**; **Li, Xuerong (1)**; LeRoy, Patrick J. (1); Yunus, Shakeeb (1); Liu, Shih-Chun (1); **Chishti, Athar H. (1)**
CS (1) Section of Hematology-Oncology Research, Departments of Medicine, Anatomy, and Cellular Biology, St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 436a. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DT Conference
LA English
AB Development of an effective subunit vaccine against **malaria** requires a precise description of the mechanism by which merozoites invade host red blood cells. Clinical manifestations and mortality in Plasmodium falciparum **malaria** are directly associated with the asexual blood stage of the parasite life cycle. An indispensable step in the blood stage is the invasion of the host red blood cell (RBC) by the circulating

merozoite. The invasion process consists of a sequence of events, during which RBC membrane proteins and merozoite coat proteins are engaged in specific receptor-ligand interactions to form unique invasion pathways. Previously, glycophorin A was identified as the sialic acid-dependent RBC receptor binding the parasite ligand EBP-175 in P. falciparum invasion. More recent evidence, however, suggests that this invasion pathway is nonessential. Here we report the identification of **erythroid band 3** as the dominant host receptor in the invasion of RBCs by Plasmodium falciparum. Using a peptide scanning strategy, two non-glycosylated exofacial regions of human **erythroid band 3** were identified as a crucial receptor. Peptides derived from the receptor region of **band 3** inhibited parasite invasion into RBCs. Parasite ligands interacting with the **band 3** receptor were identified as 38 kDa and 42 kDa domains of merozoite surface protein 1 (**MSP1**) using yeast two-hybrid and solution binding assays. Further, RBCs from **band 3** null mice were completely resistant to invasion by the **malaria** parasite. The 38 kDa and 42 kDa domains of **MSP1** bound to wild-type mouse and human RBCs, but not to the **band 3**-deficient mouse RBCs in indirect immunofluorescence assay. Together, these results reveal a novel host-parasite interaction constituting an essential **band 3**-dependent invasion pathway in **malaria** parasite's entry into host RBCs.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	65.12	65.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.65	-0.65

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 5, 2003 (20030905/UP).

=> file biosis medline agricola embase caba wpids japio biotechds lifesci caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.78	66.11

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.65

FILE 'BIOSIS' ENTERED AT 15:14:57 ON 12 SEP 2003

FILE 'MEDLINE' ENTERED AT 15:14:57 ON 12 SEP 2003

FILE 'AGRICOLA' ENTERED AT 15:14:57 ON 12 SEP 2003

FILE 'EMBASE' ENTERED AT 15:14:57 ON 12 SEP 2003

FILE 'CABA' ENTERED AT 15:14:57 ON 12 SEP 2003

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FILE 'WPIDS' ENTERED AT 15:14:57 ON 12 SEP 2003
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     FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
     LIFESCI, CAPLUS' ENTERED AT 15:01:16 ON 12 SEP 2003
                E CHISHTI ATHAR H/AU
L1          126 S E2-E3
                E LIU DAVID/AU
L2           87 S E3
                E OH S STEVEN/AU
L3          252 S E2-E3
                E GOEL VIKAS/AU
L4           24 S E3-E5
                E LI XUERONG/AU
L5           50 S E3
L6          514 S L1-L5
L7           57 S L6 AND MALARIA
L8           20 S L7 AND BAND 3
L9            9 DUP REM L8 (11 DUPLICATES REMOVED)
L10          11 S L7 AND MSP1
L11           9 S L10 AND (BAND 3 OR ERYTHROID OR ERYTHROCYTE)
L12           4 DUP REM L11 (5 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:07:15 ON 12 SEP 2003

     FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
     LIFESCI, CAPLUS' ENTERED AT 15:14:57 ON 12 SEP 2003

=> s malaria and (band 3 or erythroid or erythrocyte)
L13       9056 MALARIA AND (BAND 3 OR ERYTHROID OR ERYTHROCYTE)

=> s l13 and msp1
L14         92 L13 AND MSP1

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15          40 DUP REM L14 (52 DUPLICATES REMOVED)

=> d bib ab 1-40

L15  ANSWER 1 OF 40  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
     DUPLICATE 1
AN   2003:298699  BIOSIS
```

DN PREV200300298699
TI **Band 3** is a host receptor binding merozoite surface protein 1 during the Plasmodium falciparum invasion of erythrocytes.
AU Goel, Vikas K.; Li, Xuerong; Chen, Huiqing; Liu, Shih-Chun; Chishti, Athar H. (1); Oh, Steven S. (1)
CS (1) Department of Medicine, St. Elizabeth's Medical Center, 736 Cambridge Street, Boston, MA, 02135, USA: athar.chishti@tufts.edu, steven.oh@tufts.edu USA
SO Proceedings of the National Academy of Sciences of the United States of America, (April 29 2003) Vol. 100, No. 9, pp. 5164-5169. print.
ISSN: 0027-8424.
DT Article
LA English
AB We report the molecular identification of a sialic acid-independent host-parasite interaction in the Plasmodium falciparum **malaria** parasite invasion of RBCs. Two nonglycosylated exofacial regions of human **band 3** in the RBC membrane were identified as a crucial host receptor binding the C-terminal processing products of merozoite surface protein 1 (**MSP1**). Peptides derived from the receptor region of **band 3** inhibited the invasion of RBCs by P. falciparum. A major segment of the **band 3** receptor (5ABC) bound to native MSP142 and blocked the interaction of native MSP142 with intact RBCs in vitro. Recombinant MSP119 (the C-terminal domain of MSP142) bound to 5ABC as well as RBCs. The binding of both native MSP142 and recombinant MSP119 was not affected by the neuraminidase treatment of RBCs, but sensitive to chymotrypsin treatment. In addition, recombinant MSP138 showed similar interactions with the **band 3** receptor and RBCs, although the interaction was relatively weak. These findings suggest that the chymotrypsin-sensitive **MSP1**-**band 3** interaction plays a role in a sialic acid-independent invasion pathway and reveal the function of **MSP1** in the Plasmodium invasion of RBCs.

L15 ANSWER 2 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AN 2003:300250 BIOSIS
DN PREV200300300250
TI Crystal structure of a Fab complex formed with PfMSP1-19, the C-terminal fragment of merozoite surface protein 1 from Plasmodium falciparum: A **malaria** vaccine candidate.
AU Pizarro, J. C.; Chitarra, V.; Verger, D.; Holm, I.; Petres, S.; Dartevelle, S.; Nato, F.; Longacre, S.; Bentley, G. A. (1)
CS (1) Unite d'Immunologie Structurale (CNRS URA 2185) Departement de Biologie Structurale et Chimie, Institut Pasteur, 25 rue du Dr. Roux, 75724, Paris, cedex, 15, France: bentley@pasteur.fr France
SO Journal of Molecular Biology, (16 May 2003) Vol. 328, No. 5, pp. 1091-1103. print.
ISSN: 0022-2836.
DT Article
LA English
AB Merozoite surface protein 1 (**MSP1**) is the major protein component on the surface of the merozoite, the **erythrocyte**-invasive form of the **malaria** parasite Plasmodium. Present in all species of Plasmodium, it undergoes two distinct proteolytic maturation steps during the course of merozoite development that are essential for invasion of the **erythrocyte**. Antibodies specific for the C-terminal maturation product, **MSP1**-19, can inhibit **erythrocyte** invasion and parasite growth. This polypeptide is therefore considered to be one of the more promising **malaria** vaccine candidates. We describe here the crystal structure of recombinant **MSP1**-19 from P. falciparum (PfMSP1-19), the most virulent species of the parasite in humans, as a complex with the Fab fragment of the monoclonal antibody G17.12. This antibody recognises a discontinuous

epitope comprising 13 residues on the first epidermal growth factor (EGF)-like domain of PfMSP1-19. Although G17.12 was raised against the recombinant antigen expressed in an insect cell/baculovirus system, it binds uniformly to the surface of merozoites from the late schizont stage, showing that the cognate epitope is exposed on the naturally occurring **MSP1** polypeptide complex. Although the epitope includes residues that have been mapped to regions recognised by invasion-inhibiting antibodies studied by other workers, G17.12 does not inhibit **erythrocyte** invasion or **MSP1** processing.

L15 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:62213 CAPLUS
DN 139:83564
TI Expression, polymorphism analysis, reticulocyte binding and serological reactivity of two Plasmodium vivax MSP-1 protein recombinant fragments
AU Espinosa, Ana Maria; Sierra, Adriana Yanett; Barrero, Carlos Alberto; Cepeda, Libia Alexandra; Cantor, Elvia Maria; Lombo, Tania Bibiana; Guzman, Fanny; Avila, Sandra Julieta; Patarroyo, Manuel Alfonso
CS Fundacion Instituto de Inmunologia de Colombia, Bogota, Colombia
SO Vaccine (2003), 21(11-12), 1033-1043
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Among the four parasite species causing **malaria** in humans, Plasmodium vivax prevails on both the Asian and the American continents. Several antigens from this parasite's erythrocytic stages have been characterized and some of them are considered to be good vaccine candidates. The P. vivax merozoite surface protein-1 (PvMSP-1) is a 200 kDa antigen, thought to mediate the initial contact between the merozoite and the **erythrocyte**. An effective blockage of this interaction could be important in anti-malarial vaccine design. This study analyses the genetic polymorphism, binding to both reticulocytes and erythrocytes, antigenicity and immunogenicity of two recombinant proteins belonging to the 33 kDa PvMSP-1 proteolytic fragment. Both regions showed very low genetic variation, bound reticulocytes with higher affinity than erythrocytes, were recognized by naturally P. vivax-infected patient sera and were immunogenic when used to immunize rabbits, making them good vaccine candidates against P. vivax, to be further preclinically tested in the Aotus monkey model.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:310594 CAPLUS
DN 138:319386
TI MSP-1 **malaria** pseudopeptide analogs: Biological and immunological significance and three-dimensional structure
AU Lozano, Jose Manuel; Alba, Martha Patricia; Vanegas, Magnolia; Silva, Yolanda; Torres-Castellanos, Jose Libardo; Patarroyo, Manuel Elkin
CS Fundacion Instituto de Immunologia de Colombia (FIDIC), Bogota, Colombia
SO Biological Chemistry (2003), 384(1), 71-82
CODEN: BICHF3; ISSN: 1431-6730
PB Walter de Gruyter GmbH & Co. KG
DT Journal
LA English
AB Merozoite Surface Protein-1 (MSP-1) has been considered as a **malaria** vaccine candidate. It is processed during the Plasmodium falciparum invasion process of red blood cells (RBCs). A conserved MSP-1 C-terminal peptide was identified as a high-activity **erythrocyte** -binding peptide (HAEBP) termed 1585. Since conserved HAEBPs are neither antigenic nor immunogenic we decided to assess the significance of a single peptide bond replacement in 1585. Thus, two pseudopeptides were

WO 2002070542 A3 20030605
W: AU, BR, CA, CN, IN, JP, KR, SG, ZA
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
US 2003059436 A1 20030327 US 2002-87464 20020301
PRAI US 2001-272930P P 20010302
AB The invention provides peptides derived from **erythroid Band 3** protein, which selectively bind to merozoite surface protein-1 (MSP-1), and/or one or more of the **malaria** polypeptides: BBP-1, BBP-2, BBP-3, BBP-4, BBP-5, BBP-6, RhopH3, and ABRA and prevent infection by the parasite of a **Band 3** -expressing cell, such as an **erythrocyte**. The invention also provides the isolated polypeptides BBP-1, BBP-2, BBP-3, BBP-4, BBP-5, BBP-6, RhopH3, and/or ABRA as well as peptides derived from MSP-1, which selectively bind to **erythroid Band 3** protein and prevent parasite invasion into a **Band 3**-expressing cell, and prevent Plasmodium infection. Methods of using the **malaria** and **MSP1** polypeptides of the invention for **malaria** prevention and/or treatment (e.g. in vaccines) are also provided. Antibodies that bind to the **Band 3** polypeptides and anti-idiotypic antibodies thereto also are provided. Methods for selecting agents which inhibit **Band 3** -mediated parasite entry into target cells and methods of treatment which involve the polypeptides, antibodies, and anti-idiotypic antibodies also are provided.

L15 ANSWER 7 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 2002431963 EMBASE
TI Vaccination of monkeys with recombinant Plasmodium falciparum apical membrane antigen 1 confers protection against blood-stage **malaria** .
AU Stowers A.W.; Kennedy M.C.; Keegan B.P.; Saul A.; Long C.A.; Miller L.H.
CS A.W. Stowers, CSL Ltd., 45 Poplar Rd., Parkville, Vic. 3052, United States. anthonystowers@csl.com.au
SO Infection and Immunity, (2002) 70/12 (6961-6967).
Refs: 22
ISSN: 0019-9567 CODEN: INFIBR
CY United States
DT Journal; Article
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB A major challenge facing **malaria** vaccine development programs is identifying efficacious combinations of antigens. To date, merozoite surface protein 1 (**MSP1**) is regarded as the leading asexual vaccine candidate. Apical membrane antigen 1 (AMA1) has been identified as another leading candidate for an asexual **malaria** vaccine, but without any direct in vivo evidence that a recombinant form of Plasmodiumfalciparum AMA1 would have efficacy. We evaluated the efficacy of a form of P. falciparum AMA1, produced in Pichia pastoris, by vaccinating Aotus vociferans monkeys and then challenging them with P. falciparum parasites. Significant protection from this otherwise lethal challenge with P. falciparum was observed. Five of six animals had delayed patency; two of these remained subpatent for the course of the infection, and two controlled parasite growth at <0.75% of red blood cells parasitized. The protection induced by AMA1 was superior to that obtained with a form of **MSP1** used in the same trial. The protection induced by a combination vaccine of AMA1 and **MSP1** was not superior to the protection obtained with AMA1 alone, although the immunity generated appeared to operate against both vaccine components.

L15 ANSWER 8 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
AN 2002:495698 BIOSIS
DN PREV200200495698
TI The human immune response to Plasmodium falciparum includes both antibodies that inhibit merozoite surface protein 1 secondary processing and blocking antibodies.
AU Nwuba, Roseangela I.; Sodeinde, Olugbemiro; Anumudu, Chiaka I.; Omosun, Yusuf O.; Odaibo, Alexander B.; Holder, Anthony A. (1); Nwagwu, Mark
CS (1) Division of Parasitology, National Institute for Medical Research, The Ridgeway, Mill Hill, London, NW7 1AA: aholder@nimr.mrc.ac.uk UK
SO Infection and Immunity, (September, 2002) Vol. 70, No. 9, pp. 5328-5331. print.
ISSN: 0019-9567.
DT Article
LA English
AB **Malaria** merozoite surface protein 1 (**MSP1**) is cleaved in an essential step during **erythrocyte** invasion. The responses of children to natural **malaria** infection included antibodies that inhibit this cleavage and others that block the binding of these inhibitory antibodies. There was no correlation between the titer of the antibody to the 19-kDa fragment of **MSP1** and its inhibitory activity. These findings have implications for the design of **MSP1** -based vaccines.

L15 ANSWER 9 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4
AN 2002:304082 BIOSIS
DN PREV200200304082
TI A recombinant blood-stage **malaria** vaccine reduces Plasmodium falciparum density and exerts selective pressure on parasite populations in a phase 1-2b trial in Papua New Guinea.
AU Genton, Blaise (1); Betuela, Inoni; Felger, Ingrid; Al-Yaman, Fadwa; Anders, Robin F.; Saul, Allan; Rare, Lawrence; Baisor, Moses; Lorry, Kerry; Brown, Graham V.; Pye, David; Irving, David O.; Smith, Thomas A.; Beck, Hans-Peter; Alpers, Michael P.
CS (1) Swiss Tropical Institute, Socinstrasse 57, 4002, Basel: Blaise.genton@hospvd.ch Switzerland
SO Journal of Infectious Diseases, (15 March, 2002) Vol. 185, No. 6, pp. 820-827. print.
ISSN: 0022-1899.
DT Article
LA English
AB The **malaria** vaccine Combination B comprises recombinant Plasmodium falciparum ring-infected **erythrocyte** surface antigen and 2 merozoite surface proteins (**MSP1** and MSP2) formulated in oil-based adjuvant. A phase 1-2b double-blind, randomized, placebo-controlled trial in 120 children (5-9 years old) in Papua New Guinea demonstrated a 62% (95% confidence limits: 13%, 84%) reduction in parasite density in children not pretreated with sulfadoxine-pyrimethamine. Vaccinees had a lower prevalence of parasites carrying the MSP2-3D7 allelic form (corresponding to that in the vaccine) and a higher incidence of morbid episodes associated with FC27-type parasites. These results demonstrate functional activity of Combination B against P. falciparum in individuals with previous **malaria** exposure. The specific effects on parasites with particular msp2 genotypes suggest that the MSP2 component, at least in part, accounted for the activity. The vaccine-induced selection pressure exerted on the parasites and its consequences for morbidity strongly argue for developing vaccines comprising conserved antigens and/or multiple components covering all important allelic types.

L15 ANSWER 10 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 2002:284303 BIOSIS
DN PREV200200284303
TI Immunogenic properties of the Plasmodium vivax vaccine candidate MSP119 expressed as a secreted non-glycosylated polypeptide from Pichia pastoris.
AU Soares, I. S. (1); Rodrigues, M. M.
CS (1) UNIFESP-Escola Paulista de Medicina, Rua Botucatu 862, 6th Floor, Sao Paulo, SP, 04023-062: isoares@ecb.epm.br Brazil
SO Parasitology, (March, 2002) Vol. 124, No. 3, pp. 237-246. http://uk.cambridge.org/journals/par/. print. ISSN: 0031-1820.
DT Article
LA English
AB The 19 kDa C-terminal region of the merozoite surface protein 1 (MSP119) is one of the most promising vaccine candidates against the erythrocytic forms of **malaria**. In the present study, a gene encoding the Plasmodium vivax MSP119 epitope (PvMSP119) and the Pan-Allelic DR epitope (PADRE) was expressed in the methylotrophic yeast Pichia pastoris. A non-glycosylated form of the recombinant protein rPvMSP119-PADRE was purified from culture supernatants. This recombinant protein maintains its antigenicity, being recognized by a very high percentage (85.6%) of sera from Brazilian individuals naturally exposed to P. vivax. The antibody immune response elicited by rPvMSP119-PADRE was compared in C57BL/6 mice immunized with different adjuvant formulations. After 3 immunizing doses, antibody titres induced in the presence of the adjuvants monophosphoryl lipid A, trehalose dicorynomycolate and cell wall skeleton or alum plus CpG ODN 1826 were as high as titres generated by Complete Freund's Adjuvant. Based on these immunological studies, we concluded that rPvMSP119-PADRE deserves further evaluation in pre-clinical immunizations against P. vivax in non-human primates.

L15 ANSWER 11 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 2002070912 EMBASE
TI A DNA vaccine encoding the 42 kDa C-terminus of merozoite surface protein 1 of Plasmodium falciparum induces antibody, interferon-.gamma. and cytotoxic T cell responses in rhesus monkeys: Immuno-stimulatory effects of granulocyte macrophage-colony stimulating factor.
AU Kumar S.; Villinger F.; Oakley M.; Aguiar J.C.; Jones T.R.; Hedstrom R.C.; Gowda K.; Chute J.; Stowers A.; Kaslow D.C.; Thomas E.K.; Tine J.; Klinman D.; Hoffman S.L.; Weiss W.W.
CS S. Kumar, Merck Pharmaceutical, University of Albany, West Point, PA, United States. kumars@nmrc.navy.mil
SO Immunology Letters, (1 Apr 2002) 81/1 (13-24). Refs: 39 ISSN: 0165-2478 CODEN: IMLED6
PUI S 0165-2478(01)00316-9
CY Netherlands
DT Journal; Article
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB We have constructed a DNA plasmid vaccine encoding the C-terminal 42-kDa region of the merozoite surface protein1 (pMSP1(42)) from the 3D7 strain of Plasmodium falciparum (Pf3D7). This plasmid expressed recombinant **MSP1**(42) after in vitro transfection in mouse VM92 cells. Rhesus monkeys immunized with pMSP1(42) produced antibodies reactive with Pf3D7 infected erythrocytes by IFAT, and by ELISA against yeast produced **MSP1**(19) (yMSP1(19)). Immunization also induced antigen specific T cell responses as measured by interferon-.gamma. production, and by classical CTL chromium release assays. In addition, immunization with pMSP1(42) primed animals for an enhanced antibody response to a subsequent boost with the recombinant yMSP1(19). We also evaluated

Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF) as an adjuvant for pMSP1(42). We tested both rhesus GM-CSF expressed from a DNA plasmid, and E. coli produced recombinant human GM-CSF. Plasmids encoding rhesus GM-CSF (prhGM-CSF) and human GM-CSF (phuGM-CSF) were constructed; these plasmids expressed bio-active recombinant GMCSF. Co-immunization with a mixture of prhGM-CSF and pMSP1(42) induced higher specific antibody responses after the first dose of plasmid, but after three doses of DNA monkeys immunized with or without prhGM-CSF had the same final antibody titers and T cell responses. In comparison, rhuGM-CSF protein did not lead to accelerated antibody production after the first DNA dose. However, antibody titers were maintained at a slightly higher level in monkeys receiving GM-CSF protein, and they had a higher response to boosting with recombinant **MSP1**(19). The GM-CSF plasmid or protein appears to be less potent as an adjuvant in rhesus monkeys than each is in mice, and more work is needed to determine if GM-CSF can be a useful adjuvant in DNA vaccination of primates. .COPYRGT. 2002 Published by Elsevier Science B.V.

L15 ANSWER 12 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:335437 BIOSIS
DN PREV200300335437
TI **Band 3** Interacts with the **Malaria** Parasite Merozoite Surface Protein-1 by a Sialic Acid-Independent and Chymotrypsin-Sensitive Mechanism.
AU Oh, Steven S. (1); Li, Xuerong (1); Goel, Vikas K. (1); Chen, Huiqing (1); Liu, David S. -C. (1); Chishti, Athar H. (1)
CS (1) Departments of Medicine, Anatomy, and Cellular Biology, St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA, USA USA
SO Blood, (November 16 2002) Vol. 100, No. 11 , pp. Abstract No. 837. print. Meeting Info.: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002 American Society of Hematology . ISSN: 0006-4971.
DT Conference
LA English
AB Development of an effective subunit vaccine against blood-stage **malaria** requires a precise description of mechanism by which merozoites invade host red blood cells (RBCs). In Plasmodium falciparum **malaria**, RBC invasion is thought to proceed via two distinct routes: sialic acid-dependent and sialic acid-independent pathways. The former invasion pathway involves the interaction of the parasite ligand, EBA-175, with the sialic acid residues of host glycophorin A (GPA). Cumulative evidence using laboratory strains of P. falciparum indicate that this invasion pathway is dispensable and field isolates of P. falciparum commonly use alternate invasion pathways that do not depend on the sialic acid residues of GPA. The sialic acid-independent pathway is influenced by the trypsin-sensitive and/or chymotrypsin-sensitive RBC receptor(s). However, the molecular identity of these receptors has not been established. Recently, we have shown that the 42 kDa proteolytic fragment of P. falciparum merozoite surface protein-1 (MSP142) and its 19 kDa C-terminal domain (MSP119) bind to two non-glycosylated ectodomains of human RBC **band 3** termed 5ABC and 6A by a sialic acid-independent mechanism. Peptides derived from these ectodomains of **band 3** blocked the P. falciparum invasion of RBCs in vitro. Published evidence indicates that MSP119 plays an essential role in the blood-stage parasite development and is functionally conserved between the human and murine **malaria** parasite species. Here, we show that native P. falciparum MSP142 binds to the recombinant 5ABC peptide of **band 3** as well as to intact human RBCs in suspension. The binding of native MSP142 to RBCs was drastically reduced when 5ABC was added to the binding reaction mixture. Furthermore, native MSP142 bound to trypsin-treated, and neuraminidase-treated RBCs, but not to chymotrypsin-treated RBCs. We also show that recombinant MSP119 derived from the murine **malaria** species, P. yoelii, which shares 37%

sequence identity with P. falciparum MSP119, binds to both mouse and human intact RBCs. The chymotrypsin treatment of both RBC types showed a marked reduction in binding to P. yoelii MSP119, while the neuraminidase treatment had no effect on the binding capacity. Moreover, P. yoelii MSP119 bound to 5ABC (human sequence) that shares 98% identity with the mouse **band 3** sequence. Together, our results suggest that **band 3** is a chymotrypsin-sensitive and trypsin-insensitive RBC receptor binding the 42 kDa and 19 kDa processing products of **MSP1** during **malaria** parasite invasion of erythrocytes.

L15 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:833497 CAPLUS
DN 135:343288
TI Viral vectors encoding MSP-1 peptide of Plasmodium falciparum as vaccine against **malaria**
IN Davidson, Eugene; Nikodem, David
PA Georgetown University, USA
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085927	A1	20011115	WO 2001-US14716	20010508

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-202430P P 20000508
AB The present invention relates to a **malaria** vaccine comprising a viral vector system which expresses a protein corresponding to p115MSP-1 of the major merozoite surface antigen 1 (MSP-1) of Plasmodium falciparum or an immunogenic fragment, thereof. In preferred embodiments, the MSP-1 peptide is a 115 amino acid peptide corresponding to nucleotides 3421-3766 (West African Wellcome strain) and amino acids 1002-1116 of MSP-1. In certain aspects of the present invention, the expressed peptide may be combined with a signal peptide and/or an anchor peptide. Chimeric peptides having both signal and anchor sequences in combination with p115MSP-1 may be used. Alternative embodiments relate to methods of vaccinating patients utilizing p115MSP-1 peptides alone, or in combination with other immunogenic peptides from Plasmodium falciparum.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:246462 CAPLUS
DN 135:75489
TI Inhibitory and Blocking Monoclonal Antibody Epitopes on Merozoite Surface Protein 1 of the **Malaria** Parasite Plasmodium falciparum
AU Uthaipibull, Chairat; Aufiero, Barbara; Syed, Shabih E. H.; Hansen, Brian; Patio, Jose A. Guevara; Angov, Evelina; Ling, Irene T.; Fegeding, Konstantin; Morgan, William D.; Ockenhouse, Christian; Birdsall, Berry; Feeney, James; Lyon, Jeffery A.; Holder, Anthony A.
CS Division of Parasitology, National Institute for Medical Research, London, UK
SO Journal of Molecular Biology (2001), 307(5), 1381-1394

CODEN: JMOBAK; ISSN: 0022-2836
PB Academic Press
DT Journal
LA English
AB Merozoite surface protein 1 (MSP-1) is a precursor to major antigens on the surface of Plasmodium spp. merozoites, which are involved in **erythrocyte** binding and invasion. MSP-1 is initially processed into smaller fragments; and at the time of **erythrocyte** invasion one of these of 42 kDa (MSP-142) is subjected to a second processing, producing 33 kDa and 19 kDa fragments (MSP-133 and MSP-119). Certain MSP-1-specific monoclonal antibodies (mAbs) react with conformational epitopes contained within the two epidermal growth factor domains that comprise MSP-119, and are classified as either inhibitory (inhibit processing of MSP-142 and **erythrocyte** invasion), blocking (block the binding and function of the inhibitory mAb), or neutral (neither inhibitory nor blocking). We have mapped the epitopes for inhibitory mAbs 12.8 and 12.10, and blocking mAbs such as 1E1 and 7.5 by using site-directed mutagenesis to change specific amino acid residues in MSP-119 and abolish antibody binding, and by using PEPSCAN to measure the reaction of the antibodies with every octapeptide within MSP-142. Twenty-six individual amino acid residue changes were made and the effect of each on the binding of mAbs was assessed by Western blotting and BIAcore anal. Individual changes had either no effect, or reduced, or completely abolished the binding of individual mAbs. No two antibodies had an identical pattern of reactivity with the modified proteins. Using PEPSCAN each mAb reacted with a no. of octapeptides, most of which were derived from within the first epidermal growth factor domain, although 1E1 also reacted with peptides spanning the processing site. When the single amino acid changes and the reactive peptides were mapped onto the three-dimensional structure of MSP-119, it was apparent that the epitopes for the mAbs could be defined more fully by using a combination of both mutagenesis and PEPSCAN than by either method alone, and differences in the fine specificity of binding for all the different antibodies could be distinguished. The incorporation of several specific amino acid changes enabled the design of proteins that bound inhibitory but not blocking antibodies. These may be suitable for the development of MSP-1-based vaccines against **malaria**. (c) 2001 Academic Press.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 15 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:209830 BIOSIS
DN PREV200200209830
TI **Band 3** is a host receptor for **malaria**
parasite Plasmodium falciparum invasion of red blood cells.
AU Oh, S. Steven (1); Goel, Vikas K. (1); Li, Xuerong (1); LeRoy, Patrick J. (1); Yunus, Shakeeb (1); Liu, Shih-Chun (1); Chishti, Athar H. (1)
CS (1) Section of Hematology-Oncology Research, Departments of Medicine, Anatomy, and Cellular Biology, St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 436a.
http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DT Conference
LA English
AB Development of an effective subunit vaccine against **malaria** requires a precise description of the mechanism by which merozoites invade host red blood cells. Clinical manifestations and mortality in Plasmodium falciparum **malaria** are directly associated with the asexual blood stage of the parasite life cycle. An indispensable step in the blood stage is the invasion of the host red blood cell (RBC) by the circulating

CY United Kingdom
DT Journal; General Review
FS 004 Microbiology
026 Immunology, Serology and Transplantation
007 Pediatrics and Pediatric Surgery
030 Pharmacology
037 Drug Literature Index
017 Public Health, Social Medicine and Epidemiology
039 Pharmacy
LA English
SL English
AB The demonstration of the i) acquired protective immunity in adults living in endemic areas, ii) cure of **malaria** patients with passive transfer of specific immunoglobulins, and iii) protection conferred by vaccination with sporozoites attenuated by radiation, justifies the search for a **malaria** vaccine. Given the improbability that a vaccine directed against a single antigen will be completely protective, the preferred option is to combine several antigens of different stages of the parasite in a multi-component multi-stage vaccine which is likely to protect both travellers and populations living in endemic areas. Potential technologies include recombinant proteins, synthetic peptides and DNA vaccines, the relevant genes encoding for **malaria** antigens being inserted into a plasmid or a live vector such as vaccinia or poxvirus. A number of human trials with several antigens and technologies have been carried out in the last ten years. Three vaccines have undergone testing in the field in phase IIb or Ill trials. SPf66, including three synthetic peptides, has been extensively evaluated in different epidemiological settings. The overall efficacy was 23%, and only 2% in African infants, the most susceptible group. The circumsporozoite recombinant protein fused with the antigen S of the hepatitis B virus and formulated in a potent adjuvant (RTS,S) led to a high, but short-term, level or protection against infection and disease in Gambian adults. The first pure asexual blood-stage vaccine including three antigens of the merozoite stage (**MSP1** & 2 and RESA, Combination B) had an efficacy of 62% to reduce parasite density in Papua New Guinean children. A **malaria** vaccine that can reduce the burden of disease in the most affected populations is thus an achievable goal, each trial providing additional knowledge about mechanisms of protection as well as about vaccine technology.

L15 ANSWER 18 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5
AN 2001:510105 BIOSIS
DN PREV200100510105
TI The 22 kDa component of the protein complex on the surface of Plasmodium falciparum merozoites is derived from a larger precursor, merozoite surface protein 7.
AU Pachebat, Justin A.; Ling, Irene T.; Grainger, Munira; Trucco, Carlotta; Howell, Steven; Fernandez-Reyes, Delmiro; Gunaratne, Ruwani; Holder, Anthony A. (1)
CS (1) Division of Parasitology, National Institute for Medical Research, Mill Hill, London, NW7 1AA: aholder@nimr.mrc.ac.uk UK
SO Molecular & Biochemical Parasitology, (28 September, 2001) Vol. 117, No. 1, pp. 83-89. print.
ISSN: 0166-6851.
DT Article
LA English
SL English
AB The gene coding for merozoite surface protein 7 has been identified and sequenced in three lines of Plasmodium falciparum. The gene encodes a 351 amino acid polypeptide that is the precursor of a 22-kDa protein (MSP722) on the merozoite surface and non-covalently associated with merozoite surface protein 1 (**MSP1**) complex shed from the surface at

erythrocyte invasion. A second 19-kDa component of the complex (MSP719) was shown to be derived from MSP722 and the complete primary structure of this polypeptide was confirmed by mass spectrometry. The protein sequence contains several predicted helical and two beta elements, but has no similarity with sequences outside the Plasmodium databases. Four sites of sequence variation were identified in MSP7, all within the MSP722 region. The MSP7 gene is expressed in mature schizonts, at the same time as other merozoite surface protein genes. It is proposed that MSP722 is the result of cleavage by a protease that may also cleave **MSP1** and MSP6. A related gene was identified and cloned from the rodent **malaria** parasite, Plasmodium yoelii YM; at the amino acid level this sequence was 23% identical and 50% similar to that of P. falciparum MSP7.

L15 ANSWER 19 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 6
AN 2000:291546 BIOSIS
DN PREV200000291546
TI Safety and immunogenicity of a three-component blood-stage **malaria** vaccine in adults living in an endemic area of Papua New Guinea.
AU Genton, Blaise (1); Al-Yaman, Fadwa; Anders, Robin; Saul, Allan; Brown, Graham; Pye, David; Irving, David O.; Briggs, William R. S.; Mai, Absalom; Ginny, Meza; Adiguma, Thomas; Rare, Lawrence; Giddy, Andrew; Reber-Liske, Rosemaria; Stuerchler, Dieter; Alpers, Michael P.
CS (1) Swiss Tropical Institute, Socinstrasse 57, 4002, Basel Switzerland
SO Vaccine, (May, 2000) Vol. 18, No. 23, pp. 2504-2511. print.
ISSN: 0264-410X.
DT Article
LA English
SL English
AB A Phase I safety and immunogenicity study with a three-component blood-stage **malaria** vaccine was conducted in adult male subjects living in an endemic area of Papua New Guinea. The preparations were recombinant proteins which corresponded to parts of the two merozoite surface proteins of Plasmodium falciparum (**MSP1** and 2), and of the ring-infected **erythrocyte** surface antigen (RESA). The three proteins were emulsified with the adjuvant Montanide ISA720. Ten subjects were injected twice (four weeks apart) with the vaccine formulation and two with the adjuvant alone. Mild pain at the site of injection was reported by about half of the subjects but no systemic reaction related to the formulation occurred. There was a sharp rise in geometric mean stimulation index after the second dose compared to baseline for **MSP1** and RESA, while the rise was small for MSP2. Geometric mean antibody titres increased for **MSP1** during the study, whereas they hardly changed for MSP2 and RESA. The vaccine formulation was safe when used in an already immune population. The vaccine induced good cellular responses, especially for **MSP1** and RESA. Boosting of humoral responses was weak, probably because of high baseline antibody levels.

L15 ANSWER 20 OF 40 CABA COPYRIGHT 2003 CABI on STN DUPLICATE 7
AN 2000:81046 CABA
DN 20000807049
TI Effect of vaccination with 3 recombinant asexual-stage **malaria** antigens on initial growth rates of Plasmodium falciparum in non-immune volunteers
AU Lawrence, G.; Cheng Qin; Reed, C.; Taylor, D.; Stowers, A.; Cloonan, N.; Rzepczyk, C.; Smillie, A.; Anderson, K.; Pombo, D.; Allworth, A.; Eisen, D.; Anders, R.; Saul, A.; Cheng, Q.
CS CRC for Vaccine Technology and Australian Centre for International and Tropical Health and Nutrition, The Queensland Institute of Medical Research and The University of Queensland, Post Office, Royal Brisbane Hospital, Brisbane, Qld 4029, Australia.

SO Vaccine, (2000) Vol. 18, No. 18, pp. 1925-1931. 6 ref.
ISSN: 0264-410X
DT Journal
LA English
AB A placebo controlled randomized, double blind trial was conducted in human volunteers from Australia to test a mixture of 3 recombinant Plasmodium falciparum blood stage antigens for its ability to reduce the initial growth rates of parasites. The vaccine contained recombinant MSP2 (3D7 allele), a portion of **MSP1** (190LCS.T3) and part of the RESA antigen (C terminal 771 amino acids) in the Montanide ISA 720 adjuvant (SEPPIC). 12 volunteers received 2 doses of the vaccine, 6 weeks apart. The 5 participants in the placebo group received an equivalent volume of the adjuvant emulsion using the same schedule. Antibody responses were low, but T cell responses were stronger. All the volunteers were challenged with approximately 140 ring infected red cells of the 3D7 cloned line, 4 weeks after the 2nd dose. Parasitaemia was determined once daily from day 4 using a sensitive and quantitative polymerase chain reaction assay. All the volunteers were infected and were treated on day 8, before any developed symptoms. There was no significant difference in initial parasite growth rates between the verum and placebo groups, nor was there any significant correlation between parasite growth rates and any of the measured immunological responses. It is suggested that the formulation tested in this trial did not generate immune responses that were strong enough to reduce parasite growth in naive volunteers.

L15 ANSWER 21 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8
AN 2000:425569 BIOSIS
DN PREV200000425569
TI A principal target of human immunity to **malaria** identified by molecular population genetic and immunological analyses.
AU Conway, David J. (1); Cavanagh, David R.; Tanabe, Kazuyuki; Roper, Cally; Mikes, Zsuzsanna S.; Sakihama, Naoko; Bojang, Kalifa A.; Oduola, Ayoade M. J.; Kremsner, Peter G.; Arnot, David E.; Greenwood, Brian M.; McBride, Jana S.
CS (1) Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel St, London, WC1E 7HT UK
SO Nature Medicine, (June, 2000) Vol. 6, No. 6, pp. 689-692. print.
ISSN: 1078-8956.
DT Article
LA English
SL English
AB New strategies are required to identify the most important targets of protective immunity in complex eukaryotic pathogens. Natural selection maintains allelic variation in some antigens of the **malaria** parasite Plasmodium falciparum. Analysis of allele frequency distributions could identify the loci under most intense selection. The merozoite surface protein 1 (**Msp1**) is the most-abundant surface component on the **erythrocyte**-invading stage of P. falciparum. Immunization with whole **Msp1** has protected monkeys completely against homologous and partially against non-homologous parasite strains. The single-copy **msp1** gene, of about 5 kilobases, has highly divergent alleles with stable frequencies in endemic populations. To identify the region of **msp1** under strongest selection to maintain alleles within populations, we studied multiple intragenic sequence loci in populations in different regions of Africa and Southeast Asia. On both continents, the locus with the lowest inter-population variance in allele frequencies was block 2, indicating selection in this part of the gene. To test the hypothesis of immune selection, we undertook a large prospective longitudinal cohort study. This demonstrated that serum IgG antibodies against each of the two most frequent allelic types of block 2 of the protein were strongly associated with protection from P. falciparum **malaria**.

L15 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:659005 CAPLUS
DN 134:3793
TI Construction and immunogenicity in mice of attenuated Salmonella typhi expressing Plasmodium falciparum merozoite surface protein 1 (MSP-1) fused to tetanus toxin fragment C
AU Wu, S.; Beier, M.; Sztein, M. B.; Galen, J.; Pickett, T.; Holder, A. A.; Gomez-Duarte, O. G.; Levine, M. M.
CS Department of Medicine, Center for Vaccine Development and the Division of Geographic Medicine, University of Maryland, School of Medicine, Baltimore, MD, 21201, USA
SO Journal of Biotechnology (2000), 83(1,2), 125-135
CODEN: JBITD4; ISSN: 0168-1656
PB Elsevier Science Ltd.
DT Journal
LA English
AB One strategy to develop a multi-antigen **malaria** vaccine is to employ live vectors to carry putative protective Plasmodium falciparum antigens to the immune system. The 19 kDa carboxyl terminus of P. falciparum merozoite surface protein 1 (MSP-1), which is essential for **erythrocyte** invasion and is a leading antigen for inclusion in a multivalent **malaria** vaccine, was genetically fused to fragment C of tetanus toxin and expressed within attenuated Salmonella typhi CVD 908. Under conditions in the bacterial cytoplasm, the fragment C-MSP-1 fusion did not form the epidermal growth factor (EGF)-like domains of MSP-1; monoclonal antibodies failed to recognize these conformational domains in immunoblots of non-denatured protein extd. from live vector sonicates. The MSP-1 was nevertheless immunogenic. One month following intranasal immunization of BALB/c mice with the live vector construct, four out of five mice exhibited .gtoreq.four-fold rises in anti-MSP-1 by ELISA (GMT=211); a single intranasal booster raised titers further (GMT=1280). Post-immunization sera recognized native MSP-1 on merozoites as detd. by indirect immunofluorescence. These data encourage efforts to optimize MSP-1 expression in S. typhi (e.g. as a secreted protein), so that the EGF-like epitopes, presumably necessary for stimulating protective antibodies, can form.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 23 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 9
AN 1999:327579 BIOSIS
DN PREV199900327579
TI Plasmodium falciparum subtilisin-like protease 2, a merozoite candidate for the merozoite surface protein 1-42 maturase.
AU Barale, Jean-Christophe (1); Blisnick, Thierry; Fujioka, Hisashi; Alzari, Pedro M.; Aikawa, Masamishi; Braun-Breton, Catherine; Langsley, Gordon
CS (1) Biology of Host-Parasite Interactions Unit, Unite de Recherche Associee, Immunology Department, Centre National de la Recherche Scientifique 1960, Institut Pasteur, 25 rue du Dr. Roux, 75724, Paris Cedex 15 France
SO Proceedings of the National Academy of Sciences of the United States of America, (May 25, 1999) Vol. 96, No. 11, pp. 6445-6450.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB The process of human **erythrocyte** invasion by Plasmodium falciparum parasites involves a calcium-dependent serine protease with properties consistent with a subtilisin-like activity. This enzyme achieves the last crucial maturation step of merozoite surface protein 1 (**MSP1**) necessary for parasite entry into the host

erythrocyte. In eukaryotic cells, such processing steps are performed by subtilisin-like maturases, known as proprotein convertases. In an attempt to characterize the **MSP1** maturase, we have identified a gene that encodes a P. falciparum subtilisin-like protease (PfSUB2) whose deduced active site sequence resembles more bacterial subtilisins. Therefore, we propose that PfSUB2 belongs to a subclass of eukaryotic subtilisins different from proprotein convertases. Pfsub2 is expressed during merozoite differentiation and encodes an integral membrane protein localized in the merozoite dense granules, a secretory organelle whose contents are believed to participate in a late step of the **erythrocyte** invasion. PfSUB2's subcellular localization, together with its predicted enzymatic properties, leads us to propose that PfSUB2 could be responsible for the late **MSP1** maturation step and thus is an attractive target for the development of new antimalarial drugs.

L15 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:573319 CAPLUS
DN 132:77299
TI Human phase I vaccine trials of 3 recombinant asexual stage **malaria** antigens with Montanide ISA720 adjuvant
AU Saul, Allan; Lawrence, Gregor; Smillie, Anne; Rzepczyk, Christine M.; Reed, Carol; Taylor, Darrin; Anderson, Karen; Stowers, Anthony; Kemp, Richard; Allworth, Anthony; Anders, Robin F.; Brown, Graham V.; Pye, David; Schoofs, Peter; Irving, David O.; Dyer, Shanny L.; Woodrow, Graeme C.; Briggs, William R. S.; Reber, Rosemaria; Sturchler, Dieter
CS CRC for Vaccine Technology and Australian Centre for International and Tropical Health and Nutrition, Royal Brisbane Hospital, The Queensland Institute of Medical Research and The University of Queensland, Brisbane, 4029, Australia
SO Vaccine (1999), 17(23-24), 3145-3159
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Two phase I vaccine trials were conducted to test the immunogenicity and safety of a vaccine contg. three recombinant **malaria** antigens from the asexual stage of Plasmodium falciparum. The three antigens are a fragment of **MSP1** (190LCS.T3); MSP2 and a portion of RESA and were formulated in Montanide ISA720 adjuvant. These trials investigated the dose response of each antigen for eliciting both antibody and T-cell responses and the immunogenicity of a mixt. of the antigens compared with the antigens injected sep. All three antigens elicited both antibody and T-cell responses. Strong T-cell responses were obsd. with 190LCS.T3 and RESA with stimulation indexes exceeding 100 for peripheral blood leukocytes in some individuals. The antibody responses were generally weak. The human antibody responses obsd. with MSP2 in Montanide ISA720 were not significantly different from those obtained in an earlier trial which used MSP2 with alum as the adjuvant. No antigenic competition was obsd.: volunteers receiving a mixt. of antigens had similar responses to those receiving the three antigens at sep. sites. Tenderness and pain at the injection site were common over the first few days following immunization. In some volunteers, esp. those receiving the highest doses tested, there was a delayed reaction at the injection site with pain and swelling occurring approx. 10 days after injection.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 25 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 10
AN 1999:256332 BIOSIS
DN PREV199900256332
TI The crystal structure of C-terminal merozoite surface protein 1 at 1.8 ANG resolution, a highly protective **malaria** vaccine candidate.

AU Chitarra, Veronique; Holm, Inge; Bentley, Graham A. (1); Petres, Stephane; Longacre, Shirley
CS (1) Unite d'Immunologie Structurale (CNRS URA 1961), Institut Pasteur, 25 rue du Dr. Roux, 75724, Paris France
SO Molecular Cell, (April, 1999) Vol. 3, No. 4, pp. 457-464.
ISSN: 1097-2765.
DT Article
LA English
SL English
AB The C-terminal proteolytic processing product of merozoite surface protein 1 (**MSP1**) appears essential for successful **erythrocyte** invasion by the malarial parasite, Plasmodium. We have determined the crystal structure at 1.8 ANG resolution of a soluble baculovirus-recombinant form of the protein from P. cynomolgi, which confers excellent protective efficacy in primate vaccination trials. The structure comprises two EGF-like domains, and sequence comparisons strongly suggest that the same conformation is present in all species of Plasmodium, including P. falciparum and P. vivax, which are pathogenic in man. In particular, conserved interdomain contacts between the two EGF modules should preserve the compact form of the molecule in all species. Implications of the crystal structure for anti-malarial vaccine development are discussed.

L15 ANSWER 26 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 1999280670 EMBASE
TI Immune effector mechanisms in **malaria**.
AU Good M.F.; Doolan D.L.
CS D.L. Doolan, Malaria Program, Naval Medical Research Center, Rockville, MD 20852, United States. michaelG@qimr.edu.au
SO Current Opinion in Immunology, (1999) 11/4 (412-419).
Refs: 74
ISSN: 0952-7915 CODEN: COPIEL
CY United Kingdom
DT Journal; General Review
FS 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB **Malaria**, a disease responsible for immense human suffering, is caused by infection with Plasmodium spp. parasites, which have a very complex life cycle - antigenically unique stages infect different tissues of the body. This review details recent developments in our understanding of immunity both to pre-erythrocytic stage antigens and to erythrocytic stage antigens. The former is largely mediated via CD8+ T cells and involves IFN-.gamma., nitric oxide, IL-12 and natural killer cells; the latter varies (in different hosts and with different parasites) but is largely mediated by antibody, helper T cells, nitric oxide and .gamma..delta. T cells. The recent progress towards clinical trials of vaccine candidates against both the pre-erythrocytic stage and erythrocytic stage is also summarized, in particular the use of heterologous prime/boost strategies for the former and the use of **MSP1** as a candidate vaccine for the latter.

L15 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:56256 CAPLUS
DN 130:266022
TI An overview of **malaria** vaccine development efforts
AU Kumar, S.; Kaslow, D. C.; Hoffman, S. L.
CS Malaria Program, Naval Medical Research Institute, Rockville, MD, 20852, USA
SO Handbook of Experimental Pharmacology (1999), 133(Vaccines), 397-442
CODEN: HEPHD2; ISSN: 0171-2004
PB Springer-Verlag

DT Journal; General Review
LA English
AB A review with 270 refs. First the epidemiol. of **malaria** and the physiol. of its causative parasites in particular, Plasmodium falciparum are presented. Discussion of various approaches to **malaria** vaccine development focus on the review of vaccines against the pre-**erythrocyte** stage including the vaccines that prevent sporozoite invasion of hepatocytes or alternatively destroying the infected hepatocytes. Progress in the development of **erythrocyte** stage vaccines aimed at reducing parasite burden and blocking pathogenesis by antibodies and cytokines is also presented. Finally, some of the important parasitic antigen (such as **MSP1**, MSP2, AMA1, EBA-175, SERA, RESA) that are used in the development of the vaccines are mentioned along with a discussion of the synthetic vaccines. Pathogenesis blocking, inhibiting **malaria** toxins and transmission blocking vaccines are some addnl. strategies against **malaria** that are reviewed here.
RE.CNT 270 THERE ARE 270 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:46184 CAPLUS
DN 130:310380
TI Antibody response to the N and C-terminal regions of the Plasmodium vivax Merozoite Surface Protein 1 in individuals living in an area of exclusive transmission of P. vivax **malaria** in the north of Brazil
AU Soares, Irene S.; Oliveira, Salma G.; Souza, Jose M.; Rodrigues, Mauricio M.
CS Centro de Ciencias Biologicas, Departamento de Patologia, Universidade Federal do Para, Belem, 66075-900, Brazil
SO Acta Tropica (1999), 72(1), 13-24
CODEN: ACTRAQ; ISSN: 0001-706X
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB Recently, we found that a recombinant protein based on the 19 kDa C-terminal region of the Plasmodium vivax Merozoite Surface Protein 1 (PvMSP119) was recognized by a large proportion of individuals naturally infected. The present study was designed to det. the prevalence of antibody to PvMSP119 in individuals from the village of Cotijuba, northern Brazil, where only P. vivax transmission occurs. Immuno-epidemiol. studies on the prevalence of antibody to the C-terminus of PvMSP1 are of particular importance as this region of **MSP1** is being intensively studied as a prime candidate for development of a vaccine against **malaria**. We evaluated the antibody response to PvMSP119, and compared it to the N-terminal region of PvMSP1 and to blood stage antigens. The total frequencies of individuals with IgG to blood stages, PvMSP119 or the N-terminal region of PvMSP1 were 76.6, 42.3 and 29.8%, resp. The frequency of responders to PvMSP119 did not increase with age. However, the frequency of responders to this recombinant protein was significantly higher (77.4%) in individuals with a recent (<6 mo) history of **malaria**, when compared to subjects whose last **malaria** attack occurred more than 6 mo before (43.9%), or to individuals without a past history of symptomatic **malaria** (6.25%). These results confirm earlier studies by demonstrating that the PvMSP119 is highly immunogenic in individuals recently exposed to P. vivax **malaria**.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:743142 CAPLUS
DN 128:33532
TI Antibodies that inhibit **malaria** merozoite surface protein-1

processing and **erythrocyte** invasion are blocked by naturally acquired human antibodies

AU Patino, Jose A. Guevara; Holder, Anthony A.; Mcbride, Jana S.; Blackman, Michael J.

CS Division of Parasitology, National Institute for Medical Research, London, NW7 1AA, UK

SO Journal of Experimental Medicine (1997), 186(10), 1689-1699
CODEN: JEMEAV; ISSN: 0022-1007

PB Rockefeller University Press

DT Journal

LA English

AB Merozoite surface protein-1 (MSP-1) of the human **malaria** parasite Plasmodium falciparum undergoes at least two endoproteolytic cleavage events during merozoite maturation and release, and **erythrocyte** invasion. The authors have previously demonstrated that mAbs which inhibit **erythrocyte** invasion and are specific for epitopes within a membrane-proximal, C-terminal domain of MSP-1 (MSP-119) prevent the crit. secondary processing step which occurs on the surface of the extracellular merozoite at around the time of **erythrocyte** invasion. Certain other anti-MSP-119 mAbs, which themselves inhibit neither **erythrocyte** invasion nor MSP-1 secondary processing, block the processing-inhibitory activity of the first group of antibodies and are termed blocking antibodies. The authors have now directly quantitated antibody-mediated inhibition of MSP-1 secondary processing and invasion, and the effects on this of blocking antibodies. The authors show that blocking antibodies function by competing with the binding of processing-inhibitory antibodies to their epitopes on the merozoite. Polyclonal rabbit antibodies specific for certain MSP-1 sequences outside of MSP-119 also act as blocking antibodies. Most significantly, affinity-purified, naturally acquired human antibodies specific for epitopes within the N-terminal 83 kDa domain of MSP-1 very effectively block the processing-inhibitory activity of the anti-MSP-119 mAb 12.8. The presence of these blocking antibodies also completely abrogates the inhibitory effect of mAb 12.8 on **erythrocyte** invasion by the parasite in vitro. Blocking antibodies therefore (a) are part of the human response to malarial infection; (b) can be induced by MSP-1 structures unrelated to the MSP-119 target of processing-inhibitory antibodies; and (c) have the potential to abolish protection mediated by anti-MSP-119 antibodies. The results suggest that an effective MSP-119-based falciparum **malaria** vaccine should aim to induce an antibody response that prevents MSP-1 processing on the merozoite surface.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1996:704368 CAPLUS

DN 126:102681

TI Identification of Plasmodium falciparum MSP-1 peptides able to bind to human red blood cells

AU Urquiza, Mauricio; Rodriguez, Luis E.; Suarez, Jorge E.; Guzman, Fanny; Ocampo, Marisol; Curtidor, Hernando; Segura, Cesar; Trujillo, Esperanza; Patarroyo, Manuel E.

CS Hospital San Juan de Dios, Universidad Nacional de Colombia, Bogota, AA 44709, Colombia

SO Parasite Immunology (1996), 18(10), 515-526
CODEN: PAIMD8; ISSN: 0141-9838

PB Blackwell

DT Journal

LA English

AB To det. amino acid sequences of the P. falciparum MSP-1 protein that interact with red blood cell membranes in a specific receptor-ligand interaction, 78 sequential peptides, 20 amino acids long and spanning the

entire length of the mol., were synthesized and analyzed with a specific binding assay developed for this purpose. Results show that peptides based on conserved and dimorphic regions of MSP-1, interact with human red blood cells (RBCs). This interaction occurs predominantly with peptides contained within the MSP-1 proteolytic fragments of 83 kDa, 38 kDa, 33 kDa, and 19 kDa. Affinity consts. of these peptides were between 140 and 250 nM. Peptide-RBC binding post enzyme treatment showed that the RBC receptors are not sialic acid dependent and appear to be protein in nature. Some of these peptides inhibited merozoite invasion of RBCs yet did not inhibit intraerthrocytic development. These peptides, in conjunction with those from other merozoite surface proteins, may be used to rationally design a second generation of synthetic peptide-based **malaria** vaccines.

L15 ANSWER 31 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1996:425701 BIOSIS
DN PREV199699156757
TI Plasmodium knowlesii: Secondary processing of the **malaria** merozoite surface protein-1.
AU Blackman, Michael J. (1); Dennis, E. David; Hirst, Elizabeth M. A.; Kocken, Clemens H.; Scott-Finnigan, Terry J.; Thomas, Alan W.
CS (1) Div. Parasitol., Natl. Inst. Med. Res., The Ridgeway, Mill Hill, London NW7 1AA UK
SO Experimental Parasitology, (1996) Vol. 83, No. 2, pp. 229-239. ISSN: 0014-4894.
DT Article
LA English
AB Secondary processing of the Plasmodium falciparum **malaria** merozoite surface protein-1 (MSP-1) is defined as a single proteolytic cleavage within the carboxy-terminal membrane-bound component of the MSP-1 protein complex on the free merozoite surface. The N-terminal cleavage product (MSP-1-33) is shed from the parasite surface along with a number of other polypeptides, whereas the C-terminal processing product remains bound to the merozoite surface and is the only part of MSP-1 detectable in the newly invaded host cell. We report that secondary processing of MSP-1 takes place in a similar manner on invasive merozoites of the simian **malaria** parasite Plasmodium knowlesi. Processing can take place to a limited extent in pure isolated merozoites; however, within 10 min of the addition of purified invasive merozoites to rhesus erythrocytes, processing and shedding of **MSP1** has gone to completion only in those parasites which have undergone invasion: residual free merozoites remain uniformly reactive with antibodies against MSP-1-33. Successful invasion is therefore associated with complete shedding of MSP-1-33 from the merozoite surface. The nucleotide sequence of the 3' domain of the P. knowlesi MSP-1 gene is also presented.

L15 ANSWER 32 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 11
AN 1996:268757 BIOSIS
DN PREV199698824886
TI A single gene copy merozoite surface antigen and immune evasion.
AU O'Dea, K. P. (1); McKean, P. G.; Jarra, W.; Brown, K. N.
CS (1) Div. Parasitol., National Inst. Med. Res., Mill, London NW7 1AA UK
SO Parasite Immunology (Oxford), (1996) Vol. 18, No. 4, pp. 165-172. ISSN: 0141-9838.
DT Article
LA English
AB During the course of chronic **malaria** infection antigenic variants of a parasite antigen are expressed and exposed on the surface of infected **erythrocyte** membranes. There also exists a number of apparently invariant single gene copy blood-stage antigens, exposed or non-exposed, which have been shown to afford immunity under experimental conditions. To determine why the host, presented with invariant

'protective' antigens, is unable to control infections effectively, immunity to a representative single gene copy antigen, the merozoite surface protein 1 (**MSP1**) was investigated in Plasmodium chabaudi chabaudi AS, a murine model of chronic **malaria**. Immunization with monoclonal antibody affinity purified native **MSP1** resulted in enhanced control of parasitaemia on challenge, irrespective of the parasite inoculum size; challenge with a single parasite, however, suggested that expansion of resistant parasite subpopulations was not occurring. Challenge of mice immunized with recombinant fusion proteins encoding N- or C-terminal regions of the P.c. chabaudi AS **MSP1** produced inconsistent effects, often parasitaemias were indistinguishable from controls despite significant anti-**MSP1** antibody responses. The not unlikely contamination of **MSP1** native preparations with **erythrocyte** (E) components was considered. Immunization with a mixture of the **MSP1** C-terminus recombinant polypeptide and a Triton X-100 solubilized lysate of normal E resulted in enhanced control of parasitaemia, however, no effect was seen after administration of either component on its own. Co-immunization of E with the N-terminus polypeptide reversed the inhibition seen, on this occasion with this construct alone.

L15 ANSWER 33 OF 40 MEDLINE on STN DUPLICATE 12
AN 97213286 MEDLINE
DN 97213286 PubMed ID: 9060051
TI Clinical and parasitological studies on immunity to Plasmodium falciparum **malaria** in children.
AU Hogh B
CS Statens Serum Institut, Copenhagen, Denmark.
SO SCANDINAVIAN JOURNAL OF INFECTIOUS DISEASES. SUPPLEMENTUM, (1996) 102 1-53. Ref: 203
Journal code: 0251025. ISSN: 0300-8878.
CY Sweden
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970512
AB **Malaria** remains one of the major health problems in many tropical countries. Plasmodium falciparum is the most common **malaria** parasite in Africa, and it causes much more severe and progressive illness than any of the other types of **malaria** parasite. Children living in sub-Saharan Africa are bearing the major burden of the disease and the mortality. Whatever parameter is used to measure the mortality or the morbidity from **malaria**, the true problem is likely to be underestimated. The pattern of morbidity and mortality depends on the transmission intensity; the more intensity of **malaria** transmission is increased, the earlier and more confined the age range of symptomatic **malaria**. The asymptomatic carrier status is common, and 60-80% of the children in highly endemic areas have P. falciparum parasitaemia at any given time. Consequently a case definition based on the mere presence of parasites in the blood is non-informative in terms of measuring morbidity. Recognizing that there are no specific diagnostic clinical parameters for **malaria**, but that fever is very common, and that morbidity is to some extent dependent on the parasite density, we described using a logistic regression model the probability of being sick from **malaria** in relation to body temperature and parasite density. Acquired clinical and parasitological immunity develop progressively over several years after repeated exposure to infection. Protection is acquired first against death or severe

clinical disease, then against milder clinical attacks, but protection against infection is never complete. Clinical and parasitological immunity develop concomitantly, as demonstrated by relating the parasite densities to measured body temperature. However, the ability to control the disease and parasite density develops earlier than the ability to prevent the parasite infection. The individual immune mechanisms that are responsible for the acquired immunity remain uncertain, but classical transfer experiments with polyvalent gamma globulin from immune donors to non-immune individuals showed that antibodies play an important role. Potential targets for malarial vaccines include antigens on the surface of the sporozoites and the merozoites. Several protein antigens from P. falciparum have been characterized at the molecular level, and most of the characterized antigens have the common characteristic that they are recognized by immune sera from individuals living in **malaria** endemic areas. Working on the approach that potentially useful targets for protective vaccine development can be identified by correlating the naturally acquired immune responses with defined P. falciparum antigens, we examined antigens from both the sporozoite stage (CS-protein) and the blood stages (Pf155/RESA, GLURP, and **MSP1**), as well as P. falciparum induced neoantigens on the red blood cell (**band-3** neoantigens). The relationship between the immune response to these defined P. falciparum antigens and clinical and parasitological protection was analysed in the individual age groups. The contribution of the antigen-specific immune response was evaluated, and a positive correlation of parasite density or probability of an episode of clinical **malaria** with antibody response to the individual antigens was identified in defined age groups. This correlation, however, did not span all age groups, and thus overall responses to defined antigens are not considered to be reliable indicators of protection. The findings may contribute to the understanding of immunological and clinical host responses to parasitaemia and to defined P. falciparum antigens. The studies on the impact of asexual stage infection and the human immune response led to studies on specific and non-specific responses to P. falciparum blood-stage parasites and observations on gametocytaemia. We demonstrated that pyrimethamine/sulfadoxine and chloroquine did not induce gametocytogenesis as suggested previously, but preformed gametocytes persisted after

L15 ANSWER 34 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 13
AN 1995:130329 BIOSIS
DN PREV199598144629
TI Serum antibodies from **malaria**-exposed people recognize conserved epitopes formed by the two epidermal growth factor motifs of **MSP1**-19, the carboxy-terminal fragment of the major merozoite surface protein of Plasmodium falciparum.
AU Egan, Andrea F.; Chappel, Jonathan A.; Burghaus, Petra A.; Morris, Joanne S.; McBride, Jana S.; Holder, Anthony A.; Kaslow, David C.; Riley, Eleanor M. (1)
CS (1) Inst. Cell Animal Population Biol., Div. Biological Sci., Ashworth Lab., Univ. Edinburgh, West Mains Road, Edinburgh EH9 3JT UK
SO Infection and Immunity, (1995) Vol. 63, No. 2, pp. 456-466.
ISSN: 0019-9567.
DT Article
LA English
AB The major merozoite surface protein of Plasmodium falciparum (PfMSP1) is a candidate antigen for a **malaria** vaccine. A 19-kDa C-terminal processing product of PfMSP1 (PfMSP1-19) is composed of two domains sharing a cysteine-rich motif with epidermal growth factor (EGF) and is the target of monoclonal antibodies which block **erythrocyte** invasion in vitro. We have evaluated human antibody responses to PFMSP1-19 by using recombinant proteins representing the EGF motifs encoded by the two main alleles of the **MSP1** gene. We find that both EGF motifs

are antigenic but that only 10 to 20% of **malaria**-exposed individuals have serum antibodies that recognized either of the motifs. When both EGF motifs were expressed together as a single protein, they were recognized by more than 40% of sera from **malaria**-exposed individuals. Major epitopes recognized by human antibodies are dependent upon the correct tertiary structure of the protein and are cross-reactive between the different allelic sequences of PfMSP1-19. This suggests that antibodies induced by vaccination with one or the other allelic forms of the protein could recognize all strains of P. falciparum. Immunoglobulin G (IgG) subclass-specific enzyme immunoassays indicate that PfMSP1-19 antibodies are predominantly of the IgG1 subclass.

L15 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:250098 CAPLUS
DN 118:250098
TI A conserved region of the MSP-1 surface protein of Plasmodium falciparum contains a recognition sequence for **erythrocyte** spectrin
AU Herrera, Socrates; Rudin, Werner; Herrera, Myriam; Clavijo, Pedro; Mancilla, Lida; de Plata, Cecilia; Matile, Huges; Certa, Ulrich
CS Sch. Health, Univ. Valle, Cali, Colombia
SO EMBO Journal (1993), 12(4), 1607-14
CODEN: EMJODG; ISSN: 0261-4189
DT Journal
LA English
AB The major surface protein MSP-1 of Plasmodium faciparum blood-stage **malaria** parasites contains notably conserved sequence blocks with unknown function. The recombinant protein 190L, which represents such a block, exhibits a high affinity for red blood cell membranes. It is demonstrated that both 190L and native MSP-1 protein bind to the inner red blood cell membrane skeleton protein spectrin. By using overlapping peptides covering the 190L, it is shown that the spectrin contact site of 190L is included in a linear sequence of 30 amino acid residues. Assocn. of 190L with naturally occurring spectrin deficient red blood cells is drastically reduced. In the same cells parasite invasion is normal, but the intracellular parasite development arrests late in the trophozoite stage. A similar situation arises when synthetic peptides covering the spectrin recognition sequence of 190L are added to P. falciparum cultures. These data and the cellular localization of MSP-1 suggest the possibility that MSP-1 assocs. with spectrin under natural conditions.

L15 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:72213 CAPLUS
DN 120:72213
TI A conserved parasite serine protease processes the Plasmodium falciparum merozoite surface protein-1
AU Blackman, Michael J.; Chappel, Jonathan A.; Shai, Shafrira; Holder, Anthony A.
CS Div. Parasitol., Natl. Inst. Med. Res., London, NW7 1AA, UK
SO Molecular and Biochemical Parasitology (1993), 62(1), 103-14
CODEN: MBIPDP; ISSN: 0166-6851
DT Journal
LA English
AB The merozoite surface protein-1 of the human **malaria** parasite Plasmodium falciparum undergoes an extracellular proteolytic cleavage (secondary processing) intrinsic to successful **erythrocyte** invasion. In the T9/96 clone of P. falciparum the protease responsible has been characterized as a membrane-assocd., calcium-dependent activity, sensitive to irreversible inhibitors of serine proteases. Here the authors extend these studies and show that secondary processing activity in intact merozoites of P. falciparum strains expressing the alternative dimorphic type of merozoite surface protein-1 has identical characteristics, and that the cleavage site is close to or identical to that in the protein from T9/96. The protease responsible is shown to be

parasite-derived, and able to catalyze processing of native substrate only when present in the same membrane. Cleavage of the substrate follows apparent first order kinetics for at least 2 half-lives. It is concluded that secondary processing of both dimorphic forms of the P. falciparum merozoite surface protein-1 is a conserved event, mediated by a mechanistically conserved protease located on the merozoite surface. These observations provide clues to the identity of the protease and show that, irresp. of the dimorphic type, secondary processing results in the same, highly conserved region of the merozoite surface protein-1 remaining on th surface of the invading merozoite.

L15 ANSWER 37 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 93128561 EMBASE
DN 1993128561
TI Sequence conservation in the C-terminal part of the precursor to the major merozoite surface proteins (**MSP1**) of Plasmodium falciparum from field isolates.
AU Jongwutiwes S.; Tanabe K.; Kanbara H.
CS Department of Parasitology, Faculty of Medicine, Chulalongkorn University,Bangkok 10330, Thailand
SO Molecular and Biochemical Parasitology, (1993) 59/1 (95-100).
ISSN: 0166-6851 CODEN: MBIPDP
CY Netherlands
DT Journal; Article
FS 004 Microbiology
LA English
SL English
AB The C-terminal part of the precursor to the major merozoite surface proteinis (**MSP1**) of Plasmodium falciparum contains potential protective epitopes and two cleavage sites for processing which take place prior to **erythrocyte** invasion by the merozoite. Since sequences available to date are limited and derived from cultured parasites, we have examined the extent of variations of this important part of the **MSP1** gene from natural populations. Our sequence analyses of 1.6-1.7 kb from blocks 13-17 of the gene obtained from 19 Thai wild isolates have identified a deletion of a codon and 18 nucleotide substitutions, all of which are dimorphic substitutions and all but one create amino acid exchanges. However, residues at two cleavage sites for the C-terminus 42 kDa polypeptide and the 19-kDa polypeptide, a subfragment of the former, are conserved. Furthermore, all 12 cysteine residues at the C-terminal 19-kDa polypeptide are perfectly conserved, allowing the formation of 2 epidermal growth factor-like structures. These results indicate that in contrast to extensive variations at the N-terminal part of **MSP1**, limited variations occur at the C-terminal part.

L15 ANSWER 38 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 14
AN 1992:166736 BIOSIS
DN BA93:89061
TI SECONDARY PROCESSING OF THE PLASMODIUM-FALCIPARUM MEROZOITE SURFACE PROTEIN-1 **MSP1** BY A CALCIUM-DEPENDENT MEMBRANE-BOUND SERINE PROTEASE SHEDDING OF MSP133 AS A NONCOVALENTLY ASSOCIATED COMPLEX WITH OTHER FRAGMENTS OF THE **MSP1**.
AU BLACKMAN M J; HOLDER A A
CS DIV. PARASITOLOGY, NATIONAL INST. MED. RES., MILL HILL, LONDON NW7 1AA, UK.
SO MOL BIOCHEM PARASITOL, (1992) 50 (2), 307-316.
CODEN: MBIPDP. ISSN: 0166-6851.
FS BA; OLD
LA English
AB Merozoites of the **malaria** parasite Plasmodium falciparum possess on their surface proteolytically processed fragments of the merozoite

surface protein-1 (**MSP1**). Secondary processing of one of these fragments, MSP142, always occurs prior to, or at the point of successful **erythrocyte** reinvasion. It is shown that a product of this secondary processing, MSP133, is shed in the form of a noncovalently-associated complex with a number of other proteins, including the **MSP1**-derived species MSP138 and MSP183. Secondary processing of MSP142 is inhibited by the chelating agents ethylenediaminetetraacetic acid (EDTA) and ethyleneglycol-bis-(.beta.-aminoethyl ether)-tetraacetic acid (EGTA), and this inhibition is reversible by addition of excess calcium. Secondary processing occurs in preparations of washed, disrupted merozoites, and is inhibited by the protease inhibitors phenylmethylsulphonyl fluoride (PMSF) and diisopropyl fluorophosphate (DFP), indicating that the protease responsible is a membrane-associated serine protease.

L15 ANSWER 39 OF 40 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1992:28548 BIOSIS
DN BA93:17823
TI PROCESSING OF THE PLASMODIUM-FALCIPARUM MAJOR MEROZOITE SURFACE PROTEIN-1 IDENTIFICATION OF A 33-KILODALTON SECONDARY PROCESSING PRODUCT WHICH IS SHED PRIOR TO **ERYTHROCYTE** INVASION.
AU BLACKMAN M J; WHITTLE H; HOLDER A A
CS DIV. PARASITOL., NATIONAL INST. MED. RESEARCH, MILL HILL, LONDON NW7 1AA, UK.
SO MOL BIOCHEM PARASITOL, (1991) 49 (1), 35-44.
CODEN: MBIPDP. ISSN: 0166-6851.
FS BA; OLD
LA English
AB We have previously shown that only a single 19-kDa fragment of the Plasmodium falciparum major merozoite surface protein (**MSP1**) is carried with an invading merozoite into the infected red cell. This fragment (MSP119) is derived from the C-terminal, membrane-bound end of a major product. MSP142, of the primary stage of MSP142, of primary stage of **MSP1** proteolytic processing. Using a monoclonal antibody mapped to an epitope within the N-terminal region of MSP142, we have shown that s soluble 33-kDa polypeptide (MSP133) corresponding to the N-terminal region of MSP142 is shed into culture supernatants during merozoite release and **erythrocyte** invasion. These observations provide further evidence that the secondary processing of MSP142 involves a highly site-specific proteolytic activity.

L15 ANSWER 40 OF 40 CABA COPYRIGHT 2003 CABI on STN
AN 90:103770 CABA
DN 900866141
TI A single fragment of a **malaria** merozoite surface protein remains on the parasite during red cell invasion and is the target of invasion-inhibiting antibodies
AU Blackman, M. J.; Heidrich, H. G.; Donachie, S.; McBride, J. S.; Holder, A. A.
CS A.A. Holder, Division of Parasitology, National Institute for Medical Research, London, NW7 1AA, UK.
SO Journal of Experimental Medicine, (1990) Vol. 172, No. 1, pp. 379-382. 17 ref.
ISSN: 0022-1007
DT Journal
LA English
AB The precursor to Plasmodium falciparum major merozoite surface antigens (merozoite surface protein 1, **MSP1**) is synthesized during schizogony and is present on the merozoite as a complex of fragments derived by proteolytic processing. It was found that during **erythrocyte** invasion, only a small fragment of this complex (MSP119) is retained on the parasite surface and carried into the newly infected red cell. Antibodies to conserved epitopes on MSP119 inhibited

red cell invasion.

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FULL ESTIMATED COST	109.08	175.19

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CA SUBSCRIBER PRICE	-9.77	-10.42

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Sep 5, 2003 (20030905/UP).

SO Blood, (March 15, 1998) Vol. 91, No. 6, pp. 2146-2151.
ISSN: 0006-4971.
DT Article
LA English
AB Glycophorin A is the major transmembrane sialoglycoprotein of red blood cells. It has been shown to contribute to the expression of the MN and Wright blood group antigens, to act as a receptor for the **malaria** parasite Plasmodium falciparum and Sendai virus, and along with the anion transporter, **band 3**, may contribute to the mechanical properties of the red blood cell membrane. Several lines of evidence suggest a close interaction between glycophorin A and **band 3** during their biosynthesis. Recently, we have generated mice where the **band 3** expression was completely eliminated by selective inactivation of the AE1 anion exchanger gene, thus allowing us to study the effect of **band 3** on the expression of red blood cell membrane proteins. In this report, we show that the **band 3** -/- red blood cells contain protein 4.1, adducin, dematin, p55, and glycophorin C. In contrast, the **band 3** -/- red blood cells are completely devoid of glycophorin A (GPA), as assessed by Western blot and immunocytochemistry techniques, whereas the polymerase chain reaction (PCR) confirmed the presence of GPA mRNA. Pulse-label and pulse-chase experiments show that GPA is not incorporated in the membrane and is rapidly degraded in the cytoplasm. Based on these findings and other published evidence, we propose that **band 3** plays a chaperone-like role, which is necessary for the recruitment of GPA to the red blood cell plasma membrane.

L9 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:105507 BIOSIS
DN PREV199900105507
TI Erythroid **band 3** (-/-) mice are completely resistant to invasion by murine **malaria** Plasmodium yoelii 17XL.
AU **Oh, S. S.**; Leroy, P. J.; Hanspal, M.; Liu, S.-C.; Chishti, A. H.
CS Dep. Biomed. Res., St. Elizabeth's Med. Cent., Tufts Univ. Sch. Med., Boston, MA USA
SO Blood, (Nov. 15, 1998) Vol. 92, No. 10 SUPPL. 1 PART 1-2, pp. 4A.
Meeting Info.: 40th Annual Meeting of the American Society of Hematology Miami Beach, Florida, USA December 4-8, 1998 The American Society of Heamatology
. ISSN: 0006-4971.
DT Conference
LA English

L9 ANSWER 8 OF 9 MEDLINE on STN DUPLICATE 5
AN 97261606 MEDLINE
DN 97261606 PubMed ID: 9107533
TI Erythrocyte membrane alterations in Plasmodium falciparum **malaria** sequestration.
AU **Oh S S**; Chishti A H; Palek J; Liu S C
CS Department of Biomedical Research, St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA 02135, USA.
SO CURRENT OPINION IN HEMATOLOGY, (1997 Mar) 4 (2) 148-54. Ref: 67
Journal code: 9430802. ISSN: 1065-6251.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199706
ED Entered STN: 19970630
Last Updated on STN: 19970630
Entered Medline: 19970617

AB Plasmodium falciparum **malaria**, the most lethal form of human **malaria**, claims at least 2 million lives worldwide each year. Recently, there has been a significant advance in our understanding of the molecular basis of P. falciparum sequestration, a distinctive pathologic feature that often leads to fatal human cerebral **malaria**. Parasite-derived VAR proteins (Plasmodium falciparum-infected erythrocyte membrane protein 1) have been cloned and identified as antigenically diverse cytoadherent receptors localized to the knob protrusions that act as attachment points in parasite sequestration. Evidence now supports the hypothesis that cryptic regions of **band 3** protein are parasite-induced, host-derived erythrocyte receptors mediating parasite sequestration. Knob structures have been localized to spectrin-actin-protein 4.1 junctions in intact spread membrane skeletons. A recombinant domain of knob-associated histidine-rich protein, a major protein found in both membrane-intact and isolated knobs, has been shown to associate with filamentous actin and spectrin. Parasite- and host-derived erythrocyte membrane proteins involved in P. falciparum sequestration are discussed in this review.

L9 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 6
AN 1996:508388 BIOSIS
DN PREV199699230744
TI Targeted disruption of the murine erythroid **band 3** gene results in spherocytosis and severe haemolytic anaemia despite a normal membrane skeleton.
AU Southgate, Christopher D.; **Chishti, Athar H.**; Mitchell, Betsy; Yi, Scott J.; Palek, Jiri
CS Dep. Biomed. Res., St. Elizabeth's Med. Cent., Tufts Univ. Sch. Med., Boston, MA 02135 USA
SO Nature Genetics, (1996) Vol. 14, No. 2, pp. 227-230.
ISSN: 1061-4036.
DT Article
LA English
AB **Band 3** is the most abundant integral protein of the red blood cell membrane. It performs two critical biological functions: maintaining ionic homeostasis, by transporting Cl- and HCO-3- ions, and providing mechanical stability to the erythroid membrane. Erythroid **band 3** (AE1) is one of three anion exchangers that are encoded by separate genes. The AE1 gene is transcribed by two promoters: the upstream promoter produces erythroid **band 3**, whereas the downstream promoter initiates transcription of the **band 3** isoform in kidney. To assess the biological consequences of **band 3** deficiency, we have selectively inactivated erythroid but not kidney **band 3** by gene targeting in mice. Although no death in utero occurred, the majority of homozygous mice die within two weeks after birth. The erythroid **band 3** null mice show retarded growth, spherocytic red blood cell morphology and severe haemolytic anaemia. Remarkably, the **band 3**-/- red blood cells assembled normal membrane skeleton thus challenging the notion that the presence of **band 3** is required for the stable biogenesis of membrane skeleton. The availability of **band 3**-/- mice offers a unique opportunity to investigate the role of erythroid **band 3** in the regulation of membrane-skeletal interactions, anion transport and the invasion and growth of **malaria** parasite into red blood cells.

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obtained by introducing a Y[CH2-NH] reduced amide isoster into the 1585 crit. binding motif. The pseudopeptides bound to different HLA-DR alleles, suggesting that backbone modifications affect MHC-II binding patterns. Pseudopeptide-antibodies inhibit in vitro parasite-RBC invasion by recognizing MSP-1. Each pseudopeptide-induced antibody shows distinct recognition patterns. 1H-NMR studies demonstrated that isoster bonds modulate the pseudopeptides' structure and thus their immunol. properties, therefore representing a possible subunit **malaria** vaccine component.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:311537 CAPLUS
DN 139:132133
TI Plasmodium chabaudi chabaudi AS: modification of acute infection in CBA/Ca mice as a result of pre-treatment with **erythrocyte band 3** in adjuvant
AU O'Dea, Kieran P.; McKean, Paul G.; Neil Brown, K.
CS Department of Parasitology, National Institute for Medical Research, London, NW7 1AA, UK
SO Experimental Parasitology (2003), Volume Date 2002, 102(2), 66-71
CODEN: EXPAAA; ISSN: 0014-4894
PB Elsevier Science
DT Journal
LA English
AB In this paper, in vivo data are presented that suggest a role for host recognition of **erythrocyte band 3** in the control of **malaria** parasitemia. The course of Plasmodium chabaudi chabaudi AS acute infection in CBA/Ca mice was suppressed or enhanced as a result of treatment on two occasions with enriched prepns. of normal **erythrocyte band 3** in adjuvant. Co-treatment with **band 3** and a recombinant polypeptide encoding the C-terminal region of the P. c. chabaudi AS merozoite surface protein 1, which on its own had no clear effect on parasitemia, appeared to modulate **band 3**-induced inhibition. Despite several-fold redns. in ascending parasitemias in some **band 3**-immunized groups, there was a lack of obvious or unexpected anemia prior to, or during infection, indicating a degree of specificity in the parasitemia modifying response for infected rather than uninfected erythrocytes. These findings support a role for modified host recognition of **erythrocyte band 3** in the partial immunity that transcends phenotypic and genotypic antigenic variation by **malaria** parasites.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:696001 CAPLUS
DN 137:231370
TI **Erythroid band 3** antigenic peptides, MSP-1 protein and Plasmodium polypeptides for preventing invasion of **malaria** parasite into erythrocytes
IN Chishti, Athar H.; Oh, S. Steven; Liu, David; Goel, Vikas
PA St. Elizabeth's Medical Center, Inc., USA
SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002070542	A2	20020912	WO 2002-US6415	20020301

merozoite. The invasion process consists of a sequence of events, during which RBC membrane proteins and merozoite coat proteins are engaged in specific receptor-ligand interactions to form unique invasion pathways. Previously, glycophorin A was identified as the sialic acid-dependent RBC receptor binding the parasite ligand EBP-175 in P. falciparum invasion. More recent evidence, however, suggests that this invasion pathway is nonessential. Here we report the identification of **erythroid band 3** as the dominant host receptor in the invasion of RBCs by Plasmodium falciparum. Using a peptide scanning strategy, two non-glycosylated exofacial regions of human **erythroid band 3** were identified as a crucial receptor. Peptides derived from the receptor region of **band 3** inhibited parasite invasion into RBCs. Parasite ligands interacting with the **band 3** receptor were identified as 38 kDa and 42 kDa domains of merozoite surface protein 1 (**MSP1**) using yeast two-hybrid and solution binding assays. Further, RBCs from **band 3** null mice were completely resistant to invasion by the **malaria** parasite. The 38 kDa and 42 kDa domains of **MSP1** bound to wild-type mouse and human RBCs, but not to the **band 3**-deficient mouse RBCs in indirect immunofluorescence assay. Together, these results reveal a novel host-parasite interaction constituting an essential **band 3**-dependent invasion pathway in **malaria** parasite's entry into host RBCs.

L15 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:95997 CAPLUS
DN 134:294249
TI Isolation of a monoclonal antibody from a **malaria** patient-derived phage display library recognising the Block 2 region of Plasmodium falciparum merozoite surface protein-1
AU Sowa, K. M. P.; Cavanagh, D. R.; Creasey, A. M.; Raats, J.; McBride, J.; Sauerwein, R.; Roeffen, W. F.; Arnot, D. E.
CS Ashworth Laboratories, Animal and Population Biology, Institute of Cell, University of Edinburgh, Edinburgh, EH9 3JT, UK
SO Molecular and Biochemical Parasitology (2001), 112(1), 143-147
CODEN: MBIPDP; ISSN: 0166-6851
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB Polyclonal phage antibodies were isolated from a **malaria** patient-derived phage display library that bind to HB3 schizont Block 2 region (MAD20/B12) of the title antigen. Single Escherichia coli colonies contg. phagemids were produced from the polyclonal samples. The antibodies bound to HB3 schizont-infected erythrocytes but not to 3D7 (K1/B12-type), Wellcome (MAD20/B12-type), or RO33-type parasite-infected cells. Thus, the MAD20/B12 variant-specific but not the MAD20/B12-type-specific antigen are recognized. The DNAs for 3 of the antibodies were sequenced. Two share the same heavy and light chain sequences, and the third shares the same light chain sequence as the other 2.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 17 OF 40 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 2001415068 EMBASE
TI **Malaria** vaccines: Development of new technologies for immunisation.
AU Genton B.
CS Dr. B. Genton, Swiss Tropical Institute, Socinstrasse 57, CH-4002 Basel, Switzerland. Blaise.genton@hospvd.ch
SO CPD Infection, (2001) 2/3 (102-109).
Refs: 53
ISSN: 1468-1668 CODEN: CPDIF3

erythrocytes.

L9 ANSWER 4 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:209830 BIOSIS
DN PREV200200209830
TI **Band 3** is a host receptor for **malaria** parasite Plasmodium falciparum invasion of red blood cells.
AU **Oh, S. Steven (1)**; **Goel, Vikas K. (1)**; **Li, Xuerong (1)**; LeRoy, Patrick J. (1); Yunus, Shakeeb (1); Liu, Shih-Chun (1); **Chishti, Athar H. (1)**
CS (1) Section of Hematology-Oncology Research, Departments of Medicine, Anatomy, and Cellular Biology, St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 436a. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.
DT Conference
LA English
AB Development of an effective subunit vaccine against **malaria** requires a precise description of the mechanism by which merozoites invade host red blood cells. Clinical manifestations and mortality in Plasmodium falciparum **malaria** are directly associated with the asexual blood stage of the parasite life cycle. An indispensable step in the blood stage is the invasion of the host red blood cell (RBC) by the circulating merozoite. The invasion process consists of a sequence of events, during which RBC membrane proteins and merozoite coat proteins are engaged in specific receptor-ligand interactions to form unique invasion pathways. Previously, glycophorin A was identified as the sialic acid-dependent RBC receptor binding the parasite ligand EBP-175 in P. falciparum invasion. More recent evidence, however, suggests that this invasion pathway is nonessential. Here we report the identification of erythroid **band 3** as the dominant host receptor in the invasion of RBCs by Plasmodium falciparum. Using a peptide scanning strategy, two non-glycosylated exofacial regions of human erythroid **band 3** were identified as a crucial receptor. Peptides derived from the receptor region of **band 3** inhibited parasite invasion into RBCs. Parasite ligands interacting with the **band 3** receptor were identified as 38 kDa and 42 kDa domains of merozoite surface protein 1 (MSP1) using yeast two-hybrid and solution binding assays. Further, RBCs from **band 3** null mice were completely resistant to invasion by the **malaria** parasite. The 38 kDa and 42 kDa domains of MSP1 bound to wild-type mouse and human RBCs, but not to the **band 3**-deficient mouse RBCs in indirect immunofluorescence assay. Together, these results reveal a novel host-parasite interaction constituting an essential **band 3**-dependent invasion pathway in **malaria** parasite's entry into host RBCs.

L9 ANSWER 5 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
AN 2000:520647 BIOSIS
DN PREV200000520647
TI A cysteine protease activity from Plasmodium falciparum cleaves human erythrocyte ankyrin.
AU Raphael, Primrose; Takakuwa, Yuichi; Manno, Sumie; Liu, Shih-Chun; **Chishti, Athar H.**; Hanspal, Manjit (1)
CS (1) Division of Hematology Research, Departments of Medicine, Anatomy and Cellular Biology, ACH 406, St Elizabeth's Medical Center of Boston, Tufts University School of Medicine, Boston, MA, 02135 USA
SO Molecular and Biochemical Parasitology, (October, 2000) Vol. 110, No. 2, pp. 259-272. print.
ISSN: 0166-6851.
DT Article
LA English

L9 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:335437 BIOSIS
DN PREV200300335437
TI **Band 3** Interacts with the **Malaria** Parasite Merozoite Surface Protein-1 by a Sialic Acid-Independent and Chymotrypsin-Sensitive Mechanism.
AU Oh, Steven S. (1); **Li, Xuerong (1)**; **Goel, Vikas K. (1)**; Chen, Huiqing (1); Liu, David S. -C. (1); **Chishti, Athar H. (1)**
CS (1) Departments of Medicine, Anatomy, and Cellular Biology, St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA, USA USA
SO Blood, (November 16 2002) Vol. 100, No. 11 , pp. Abstract No. 837. print. Meeting Info.: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002 American Society of Hematology . ISSN: 0006-4971.
DT Conference
LA English
AB Development of an effective subunit vaccine against blood-stage **malaria** requires a precise description of mechanism by which merozoites invade host red blood cells (RBCs). In Plasmodium falciparum **malaria**, RBC invasion is thought to proceed via two distinct routes: sialic acid-dependent and sialic acid-independent pathways. The former invasion pathway involves the interaction of the parasite ligand, EBA-175, with the sialic acid residues of host glycophorin A (GPA). Cumulative evidence using laboratory strains of P. falciparum indicate that this invasion pathway is dispensable and field isolates of P. falciparum commonly use alternate invasion pathways that do not depend on the sialic acid residues of GPA. The sialic acid-independent pathway is influenced by the trypsin-sensitive and/or chymotrypsin-sensitive RBC receptor(s). However, the molecular identity of these receptors has not been established. Recently, we have shown that the 42 kDa proteolytic fragment of P. falciparum merozoite surface protein-1 (MSP142) and its 19 kDa C-terminal domain (MSP119) bind to two non-glycosylated ectodomains of human RBC **band 3** termed 5ABC and 6A by a sialic acid-independent mechanism. Peptides derived from these ectodomains of **band 3** blocked the P. falciparum invasion of RBCs in vitro. Published evidence indicates that MSP119 plays an essential role in the blood-stage parasite development and is functionally conserved between the human and murine **malaria** parasite species. Here, we show that native P. falciparum MSP142 binds to the recombinant 5ABC peptide of **band 3** as well as to intact human RBCs in suspension. The binding of native MSP142 to RBCs was drastically reduced when 5ABC was added to the binding reaction mixture. Furthermore, native MSP142 bound to trypsin-treated, and neuraminidase-treated RBCs, but not to chymotrypsin-treated RBCs. We also show that recombinant MSP119 derived from the murine **malaria** species, P. yoelii, which shares 37% sequence identity with P. falciparum MSP119, binds to both mouse and human intact RBCs. The chymotrypsin treatment of both RBC types showed a marked reduction in binding to P. yoelii MSP119, while the neuraminidase treatment had no effect on the binding capacity. Moreover, P. yoelii MSP119 bound to 5ABC (human sequence) that shares 98% identity with the mouse **band 3** sequence. Together, our results suggest that **band 3** is a chymotrypsin-sensitive and trypsin-insensitive RBC receptor binding the 42 kDa and 19 kDa processing products of MSP1 during **malaria** parasite invasion of erythrocytes.

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Research, Departments of Medicine,

the **band 3**-deficient mouse RBCs in indirect immunofluorescence assay. Together, these results reveal a novel host-parasite interaction constituting an essential **band 3**-dependent invasion pathway in **malaria** parasite's entry into host RBCs.

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DUPLICATE 3
AN 2000:520647 BIOSIS
DN PREV200000520647
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AU Raphael, Primrose; Takakuwa, Yuichi; Manno, Sumie; Liu, Shih-Chun; **Chishti, Athar H.**; Hanspal, Manjit (1)
CS (1) Division of Hematology Research, Departments of Medicine, Anatomy and Cellular Biology, ACH 406, St Elizabeth's Medical Center of Boston, Tufts University School of Medicine, Boston, MA, 02135 USA
SO Molecular and Biochemical Parasitology, (October, 2000) Vol. 110, No. 2, pp. 259-272. print.
ISSN: 0166-6851.
DT Article
LA English
SL English
AB The **malaria** parasite Plasmodium falciparum undergoes distinct morphologic changes during its 48-h life cycle inside human red blood cells. Parasite proteinases appear to play important roles at all stages of the erythrocytic cycle of human **malaria**. Proteases involved in erythrocyte rupture and invasion are possibly required to breakdown erythrocyte membrane skeleton. To identify such proteases, soluble cytosolic extract of isolated trophozoites/schizonts was incubated with erythrocyte membrane ghosts or spectrin-actin depleted inside-out vesicles, which were then analyzed by SDS-PAGE. In both cases, a new protein band of 155 kDa was detected. The N-terminal peptide sequencing established that the 155 kDa band represents truncated ankyrin. Immunoblot analysis using defined monoclonal antibodies confirmed that ankyrin was cleaved at the C-terminus. While the enzyme preferentially cleaved ankyrin, degradation of protein 4.1 was also observed at high concentrations of the enzyme. The optimal activity of the purified enzyme, using ankyrin as substrate, was observed at pH 7.0-7.5, and the activity was strongly inhibited by standard inhibitors of cysteine proteinases (cystatin, NEM, leupeptin, E-64 and MDL 28 170), but not by inhibitors of aspartic (pepstatin) or serine (PMSF, DFP) proteinases. Furthermore, we demonstrate that protease digestion of ankyrin substantially reduces its interaction with ankyrin-depleted membrane vesicles. Ektacytometric measurements showed a dramatic increase in the rate of fragmentation of ghosts after treatment with the protease. Although the role of ankyrin cleavage in vivo remains to be determined, based on our findings we postulate that the parasite-derived cysteine protease activity cleaves host ankyrin thus weakening the ankyrin-**band 3** binding interactions and destabilizing the erythrocyte membrane skeleton, which, in turn, facilitates parasite release. Further characterization of the enzyme may lead to the development of novel antimalarial drugs.

L9 ANSWER 6 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4
AN 1998:175919 BIOSIS
DN PREV199800175919
TI Complete deficiency of glycophorin A in red blood cells from mice with targeted inactivation of the **band 3** (AE1) gene.
AU Hassoun, Hani; Hanada, Toshihiko; Lutchman, Mohini; Sahr, Kenneth E.; Palek, Jiri; Hanspal, Manjit; **Chishti, Athar H. (1)**
CS (1) ACH4 Build., St. Elizabeth's Med. Cent., 736 Cambridge St., Boston, MA 02135 USA

vitro. Published evidence indicates that MSP119 plays an essential role in the blood-stage parasite development and is functionally conserved between the human and murine **malaria** parasite species. Here, we show that native P. falciparum MSP142 binds to the recombinant 5ABC peptide of **band 3** as well as to intact human RBCs in suspension. The binding of native MSP142 to RBCs was drastically reduced when 5ABC was added to the binding reaction mixture. Furthermore, native MSP142 bound to trypsin-treated, and neuraminidase-treated RBCs, but not to chymotrypsin-treated RBCs. We also show that recombinant MSP119 derived from the murine **malaria** species, P. yoelii, which shares 37% sequence identity with P. falciparum MSP119, binds to both mouse and human intact RBCs. The chymotrypsin treatment of both RBC types showed a marked reduction in binding to P. yoelii MSP119, while the neuraminidase treatment had no effect on the binding capacity. Moreover, P. yoelii MSP119 bound to 5ABC (human sequence) that shares 98% identity with the mouse **band 3** sequence. Together, our results suggest that **band 3** is a chymotrypsin-sensitive and trypsin-insensitive RBC receptor binding the 42 kDa and 19 kDa processing products of MSP1 during **malaria** parasite invasion of erythrocytes.

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SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 436a. http://www.bloodjournal.org/. print.
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administering a pharmaceutical composition of (35) to prevent or treat the malaria infection;

(37) an isolated nucleic acid molecule;

(38) an isolated nucleic acid molecule comprising a unique fragment;

(39) an expression vector comprising the isolated nucleic acid of (37) operably linked to a promoter; and

(40) an isolated polypeptide molecule comprising a unique fragment of a 743 residue amino acid sequence, given in the specification, that binds to a Band 3 polypeptide.

ACTIVITY - Protozoacide.

MECHANISM OF ACTION - Gene therapy; Vaccine.

The blot overlay results provide evidence that Band 3 functions as a receptor in the Plasmodium falciparum invasion of red blood cells (RBC), and suggest that the underlying mechanism for the observed inhibition of invasion involves a specific binding of the Band 3 peptides to one or more merozite ligands, thus competitively blocking its interaction with the RBC Band 3 receptor.

USE - The methods and compositions of the present invention are useful for the prevention and treatment of malarial infection.

ADVANTAGE - The present invention, compared to prior art, develops new and more improved methods based upon inhibiting the particular interactions between the malarial parasite and a cognate molecule present in the host, and subsequently minimizing harmful side effects and drug resistance that may be due to non-specific therapeutic approaches. The present invention also provides a vaccine for malaria.

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L9 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 2003:335437 BIOSIS

DN PREV200300335437

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CS (1) Departments of Medicine, Anatomy, and Cellular Biology, St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA, USA USA

SO Blood, (November 16 2002) Vol. 100, No. 11 , pp. Abstract No. 837. print. Meeting Info.: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002 American Society of Hematology . ISSN: 0006-4971.

DT Conference

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